Paula

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=> d his ful
     FILE 'HCAPLUS' ENTERED AT 15:40:00 ON 30 JAN 2007
                E 180916-16-9/RN
L1            1 SEA ABB=ON  PLU=ON  180916-16-9/RN
                D STAT QUE L1
                D IDE CAN L1

     FILE 'HCAPLUS' ENTERED AT 15:41:36 ON 30 JAN 2007

     FILE 'REGISTRY' ENTERED AT 15:42:20 ON 30 JAN 2007
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L2              SEL PLU=ON  L1 1- CHEM :       2 TERMS
                SET SMARTSELECT OFF

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L3          136 SEA ABB=ON  PLU=ON  L2
L4            0 SEA ABB=ON  PLU=ON  L3 AND (INFLAMMATORY(W)BOWEL OR IBD)
                D STAT QUE L4
L5       260272 SEA ABB=ON  PLU=ON  ("INFLAMMATORY BOWEL DISEASE"/CV OR
                "INTESTINE, DISEASE (L) INFLAMMATORY"/CV) OR BOWEL OR INTESTIN?
L6           16 SEA ABB=ON  PLU=ON  L3 AND L5
L7            1 SEA ABB=ON  PLU=ON  L3(L)?INFLAMM?
L8           17 SEA ABB=ON  PLU=ON  L6 OR L7
                D STAT QUE L8
                D IBIB ABS HITSTR L8 1-17
L12         262 SEA ABB=ON  PLU=ON  ("MACLEAN DAVID"/AU OR "MACLEAN DAVID
                A"/AU OR "MACLEAN DAVID B"/AU OR "MACLEAN DAVID BAILEY"/AU OR
                "MACLEAN DAVID BARKER"/AU OR "MACLEAN DAVID BURTON"/AU) OR
                MACLEAN D/AU OR MACLEAN D B/AU
L13         421 SEA ABB=ON  PLU=ON  THOMPSON D/AU OR THOMPSON D D/AU OR
                "THOMPSON DAVID"/AU OR ("THOMPSON DAVID D"/AU OR "THOMPSON
                DAVID DUANE"/AU)
L14          20 SEA ABB=ON  PLU=ON  L12 AND L13
L15          25 SEA ABB=ON  PLU=ON  (L12 OR L13) AND L3
L16          11 SEA ABB=ON  PLU=ON  (L12 OR L13) AND L5
L17          49 SEA ABB=ON  PLU=ON  L14 OR L15 OR L16
L18          46 SEA ABB=ON  PLU=ON  L17 NOT L8
                D STAT QUE L18
                D IBIB ABS HITSTR L18 1-46


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   29 JAN 2007  HIGHEST RN 918776-45-1
     DICTIONARY FILE UPDATES:  29 JAN 2007  HIGHEST RN 918776-45-1

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS



FILE COVERS 1907 - 30 Jan 2007 VOL 146 ISS 6
FILE LAST UPDATED: 29 Jan 2007 (20070129/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=> fil reg
FILE 'REGISTRY' ENTERED AT 15:41:12 ON 30 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 JAN 2007 HIGHEST RN 918776-45-1
DICTIONARY FILE UPDATES: 29 JAN 2007 HIGHEST RN 918776-45-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
=>

=> => d stat que l1

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L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  180916-16-9/RN


=> d ide can l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   180916-16-9  REGISTRY
ED   Entered STN:  18 Sep 1996
CN   2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-
     pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-
     pyrrolidinyl)ethoxy]phenyl]-, (5R-cis)-
OTHER NAMES:
CN   Lasofoxifene
FS   STEREOSEARCH
MF   C28 H31 N O2
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, DDFU,
       DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, PROUSDDR,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

Absolute stereochemistry.  Rotation (-).
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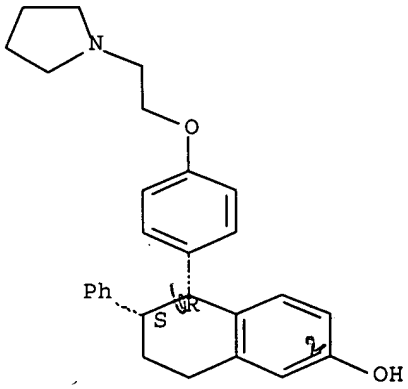


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             122 REFERENCES IN FILE CA (1907 TO DATE)
               7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             122 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE   1:  146:74355

REFERENCE   2:  146:19295

REFERENCE   3:  145:483657

REFERENCE   4:  145:465947
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REFERENCE   5:  145:262315

REFERENCE   6:  145:240583

REFERENCE   7:  145:225326

REFERENCE   8:  145:20362

REFERENCE   9:  145:944

REFERENCE  10:  145:252


=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:41:36 ON 30 JAN 2007
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FILE COVERS 1907 - 30 Jan 2007  VOL 146 ISS 6
FILE LAST UPDATED: 29 Jan 2007  (20070129/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> => d stat que l4
L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  180916-16-9/RN
L2               SEL  PLU=ON  L1 1- CHEM :       2 TERMS
L3           136 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L4             0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND (INFLAMMATORY(W)BOWEL
                 OR IBD)


=>
=> d stat que l8
L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  180916-16-9/RN
L2               SEL  PLU=ON  L1 1- CHEM :       2 TERMS
L3           136 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L5        260272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("INFLAMMATORY BOWEL DISEASE"/
                 CV OR "INTESTINE, DISEASE (L) INFLAMMATORY"/CV) OR BOWEL OR
                 INTESTIN?
L6            16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L5
L7             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(L)?INFLAMM?
L8            17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 OR L7
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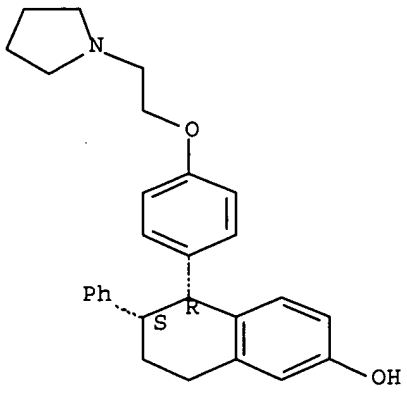
L8 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:971035 HCAPLUS Full-text
DOCUMENT NUMBER: 146:74355
TITLE: Lasofoxifene: a new type of selective estrogen receptor modulator for the treatment of osteoporosis
AUTHOR(S): Gennari, Luigi
CORPORATE SOURCE: Department of Internal Medicine, Endocrine-Metabolic Sciences and Biochemistry, Policlinico Le Scotte, University of Siena, Siena, Italy
SOURCE: Drugs of Today (2006), 42(6), 355-367
CODEN: MDACAP; ISSN: 1699-3993
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Selective estrogen receptor modulators (SERMs) are structurally different compds. that interact with intracellular estrogen receptors in target organs as estrogen agonists and antagonists. Thus far SERMs have proven to be a highly versatile group and are being evaluated primarily for conditions associated with aging, including hormone-responsive cancer and osteoporosis. Tamoxifen and toremifene are currently used to treat advanced breast cancer and also have beneficial effects on bone mineral d. and serum lipids in post-menopausal women. Raloxifene is the only SERM compound actually approved worldwide for the prevention and treatment of postmenopausal osteoporosis and fragility fractures. Unfortunately, although these SERMs possess many benefits, they are also responsible for some very serious side effects, such as thromboembolic disorders and, in the case of tamoxifen, uterine cancer. These contraindications represent a major concern for the type of long-term, chronic therapy that is required to prevent osteoporosis. Moreover, both preclin. and clin. reports suggest that these SERMs are considerably less potent than estrogen, probably due to their reduced bioavailability. Lasofoxifene (CP 336,156) is a naphthalene-derivative, third-generation SERM, structurally distinct from the first- and second-generation SERMs. This compound selectively binds to both estrogen receptor subtypes (estrogen receptor-alpha or -beta) with high affinity. It has a half-inhibition concentration similar to that seen with estradiol and thus at least 10-fold higher than those reported for raloxifene and tamoxifen. Moreover, due to increased resistance to intestinal wall glucuronidation, lasofoxifene has a remarkably improved oral bioavailability with respect to other SERMs. In both preclin. and short-term clin. studies lasofoxifene has shown a proven efficacy in preventing bone loss and lowering cholesterol levels. Dose modeling from phase II studies allowed the selection of lasofoxifene 0.25 mg/day as the lowest fully ED. The compound shows a favorable safety profile and is currently in phase III development for the prevention and treatment of osteoporosis in post-menopausal women.

IT 180916-16-9, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene was safe and effective for treatment of osteoporosis in postmenopausal woman)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

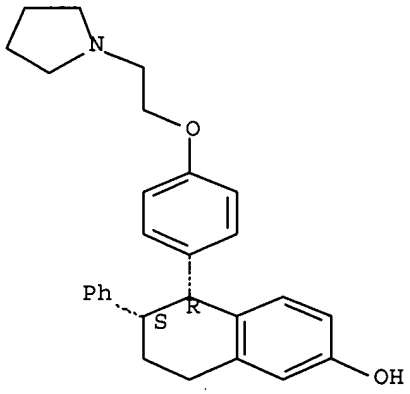
L8 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:818823 HCAPLUS Full-text
DOCUMENT NUMBER: 145:262315
TITLE: Lasofoxifene: a third-generation selective estrogen receptor modulator for the prevention and treatment of osteoporosis
AUTHOR(S): Gennari, Luigi; Merlotti, Daniela; Martini, Giuseppe; Nuti, Ranuccio
CORPORATE SOURCE: University of Siena, Endocrine-Metabolic Sciences and Biochemistry, Department of Internal Medicine, Siena, 53100, Italy
SOURCE: Expert Opinion on Investigational Drugs (2006), 15(9), 1091-1103
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. This article reviews lasofoxifene, a new-generation selective estrogen receptor modulator (SERM) that is currently in Phase III development for the prevention and treatment of osteoporosis in postmenopausal women. This compound selectively binds to both of the estrogen receptors with a high affinity and a median inhibitory concentration that is similar to that seen with estradiol and ≥ 10-fold higher than those reported for other SERMs (raloxifene and tamoxifen). Lasofoxifene has a remarkably improved oral bioavailability with respect to other SERMs due to increased resistance to intestinal wall glucuronidation. In both preclin. and short-term studies, the compound showed a favorable safety profile and demonstrated a proven efficacy in preventing bone loss and lowering cholesterol levels. Dose modeling from Phase II studies allowed the selection of lasofoxifene 0.25 mg/day as the lowest fully ED.

IT 180916-16-9, Lasofoxifene
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene, a third-generation selective estrogen receptor modulator for prevention and treatment of osteoporosis)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1354726 HCAPLUS Full-text
DOCUMENT NUMBER: 144:81225
TITLE: 5-LOX inhibitors and bone and cartilage beneficial agent combinations for arthritis, osteoporosis, or pain
INVENTOR(S): Christgau, Stephan; Hansen, Christian; Nilsson, Henrik
PATENT ASSIGNEE(S): Osteologix A/S, Den.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005123130 | A2 | 20051229 | WO 2005-DK403 | 20050617 |
| WO 2005123130 | A3 | 20060202 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2004-948 A 20040617

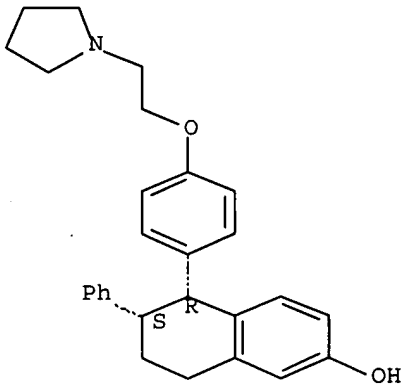
AB Combination treatments, wherein a 5-lipoxygenase (5-LOX) inhibitor are administered together with a bone or cartilage beneficial compound in order to obtain a therapeutically beneficial effect in the treatment and/or prophylaxis of osteoarthritis, rheumatoid arthritis, osteoporosis or pain, and pharmaceutical compns. comprising a combination of a 5-LOX inhibitor and a bone and cartilage beneficial compound

IT 180916-16-9, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-LOX inhibitor and bone and cartilage beneficial agent combinations for arthritis, osteoporosis, or pain)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1239173 HCAPLUS Full-text

DOCUMENT NUMBER: 143:477963

TITLE: Preparation of pyrazolyl urea derivatives as TrkA kinase inhibitors useful in the treatment of cancer

INVENTOR(S): Lee, Wendy; Ladouceur, Gaetan; Dumas, Jacques; Smith, Roger; Ying, Shihong; Wang, Gan; Chen, Zhi; Liu, Qingjie; Mokdad, Holia Hatoum

PATENT ASSIGNEE(S): Bayer Pharmacueticals Corporation, USA

SOURCE: PCT Int. Appl., 215 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005110994 | A2 | 20051124 | WO 2005-US15106 | 20050502 |
| WO 2005110994 | A3 | 20060202 | | |
| WO 2005110994 | A8 | 20061221 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
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RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

CA 2564325 A1 20051124 CA 2005-2564325 20050502
PRIORITY APPLN. INFO.: US 2004-566445P P 20040430
WO 2005-US15106 W 20050502

OTHER SOURCE(S): MARPAT 143:477963
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

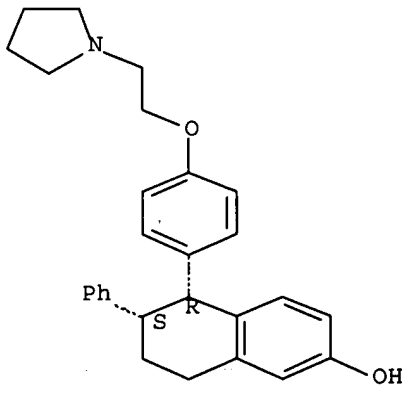
AB Title compds. I [R1-2 = H, alkyl, halo; A = Ph, pyridine, pyrimidine; B = phenylene, naphthylene; L = O, S, CH2; M = Ph, pyridine, pyrimidine; n = 0-1; X = O, SO2, etc.; Y = alkoxy, oxycarbonyl, amino, etc.] are prepared For instance, II is prepared from 4-[3-tert-butyl-5-[N'-[4-(pyridin-4-yloxy)phenyl]ureido]pyrazol-1-yl]benzoic acid Me ester (preparation given) and 2-(pyrrolidin-1-yl)ethylamine (DCE, AlMe3, 80°, 16 h). Compds. of the invention show significant inhibition of TrkA kinase (IC50 < 1 μM). I are useful for the treatment of cancer.

IT 180916-16-9, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted pyrazolylurea derivs. useful for cancer treatment)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:490384 HCAPLUS Full-text
DOCUMENT NUMBER: 143:42681
TITLE: Anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer
INVENTOR(S): Wang, Yan; Pachter, Jonathan A.; Bishop, Walter R.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005052005 | A1 | 20050609 | WO 2004-US38842 | 20041119 |
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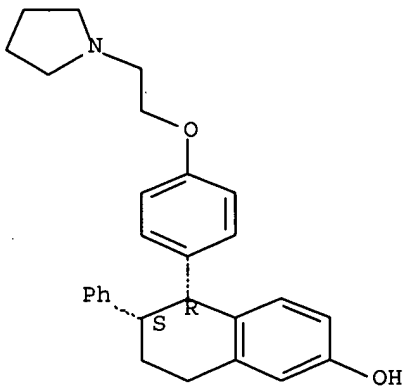
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004292554 | A1 | 20050609 | AU 2004-292554 | 20041119 |
| CA 2546664 | A1 | 20050609 | CA 2004-2546664 | 20041119 |
| US 2005136063 | A1 | 20050623 | US 2004-993395 | 20041119 |
| EP 1689782 | A1 | 20060816 | EP 2004-811545 | 20041119 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU | | | | |
| NO 2006002885 | A | 20060818 | NO 2006-2885 | 20060620 |
| PRIORITY APPLN. INFO.: | | | US 2003-524732P P | 20031121 |
| | | | WO 2004-US38842 W | 20041119 |

AB The present invention provides combinations including a binding composition, such as an anti-IGFR1 antibody, in association with a chemotherapeutic agent. The antibody is e.g. a human monoclonal antibody recognizing human IGFR-1, especially soluble IGFR-1. The chemotherapeutic agent is selected from a taxane, topoisomerase inhibitor, signal transduction inhibitor, cell cycle inhibitor, farnesyl protein transferase inhibitor, EGFR inhibitor, HER2 inhibitor, VEGFR inhibitor, MAP kinase inhibitor, MEK kinase inhibitor, AKT kinase inhibitor, mTOR inhibitor, etc. Methods for using the combinations to treat medical conditions, such as cancer, are also provided.

IT 180916-16-9, Lasofoxifene
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:470251 HCAPLUS Full-text
DOCUMENT NUMBER: 143:19957
TITLE: Combination therapy comprising a cyclooxygenase 2 (COX-2) inhibitor and an antineoplastic agent for treatment or prevention of neoplasia
INVENTOR(S): Masferrer, Jaime L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 317 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005048942 | A2 | 20050602 | WO 2004-US38019 | 20041115 |
| WO 2005048942 | A3 | 20060330 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005227929 | A1 | 20051013 | US 2004-989192 | 20041115 |
| PRIORITY APPLN. INFO.: | | | US 2003-519701P | P 20031113 |

AB A method for treating or preventing neoplasia or a neoplasia-related disorder in a subject is provided, the method comprising administering to the subject an effective amount of a combination comprising a COX-2 inhibitor and an antineoplastic agent.

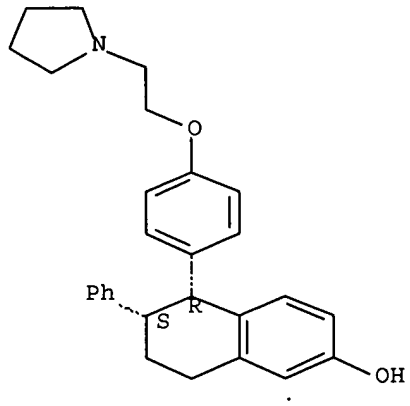
IT 180916-16-9, Lasofoxifene
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:995989 HCAPLUS Full-text

DOCUMENT NUMBER: 142:747

TITLE: Combination treatment with strontium for the prophylaxis and/or treatment of cartilage and/or bone conditions

INVENTOR(S): Hansen, Christian; Nilsson, Henrik

PATENT ASSIGNEE(S): Nordic Bone A/S, Den.; Osteologix A/S; Christgau, Stephan

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098618 | A2 | 20041118 | WO 2004-DK327 | 20040506 |
| WO 2004098618 | A3 | 20050324 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004237438 | A1 | 20041118 | AU 2004-237438 | 20040506 |

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|---|---|---|---|---|---|
| CA 2524610 | A1 | 20041118 | CA 2004-2524610 | | 20040506 |
| EP 1622630 | A2 | 20060208 | EP 2004-731315 | | 20040506 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | | |
| JP 2006525242 | T | 20061109 | JP 2006-504378 | | 20040506 |
| EP 1745791 | A2 | 20070124 | EP 2006-21612 | | 20040506 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK | | | | | |
| AU 2005240257 | A1 | 20051117 | AU 2005-240257 | | 20050505 |
| CA 2565840 | A1 | 20051117 | CA 2005-2565840 | | 20050505 |
| WO 2005108339 | A2 | 20051117 | WO 2005-DK307 | | 20050505 |
| WO 2005108339 | A3 | 20051229 | | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| EP 1744770 | A2 | 20070124 | EP 2005-734804 | | 20050505 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | | |
| US 2006275503 | A1 | 20061207 | US 2006-556149 | | 20060720 |
| PRIORITY APPLN. INFO.: | | | DK 2003-691 | A | 20030507 |
| | | | DK 2003-931 | A | 20030620 |
| | | | DK 2003-1819 | A | 20031209 |
| | | | US 2003-528548P | P | 20031209 |
| | | | DK 2003-932 | A | 20030620 |
| | | | DK 2003-1820 | A | 20031209 |
| | | | US 2003-528442P | P | 20031209 |
| | | | EP 2004-731317 | A3 | 20040506 |
| | | | WO 2004-DK326 | W | 20040506 |
| | | | WO 2004-DK327 | W | 20040506 |
| | | | WO 2004-DK328 | W | 20040506 |
| | | | DK 2004-1708 | A | 20041105 |
| | | | WO 2005-DK307 | W | 20050505 |

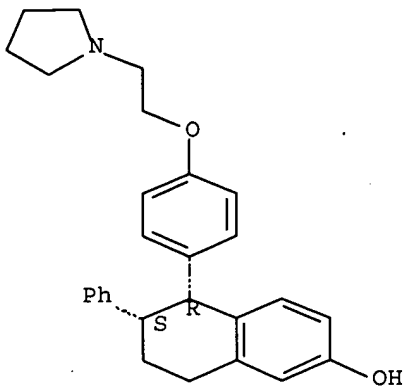
AB A combination treatment, wherein a strontium-containing compound together with one or more active substances capable of reducing the incidence of bone fracture and/or increasing bone d. and/or improving healing of fractured bone and/or improving bone quality are administered for use in the treatment and/or prophylaxis of cartilage and/or bone conditions.

IT 180916-16-9, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:759835 HCAPLUS Full-text
DOCUMENT NUMBER: 141:277616
TITLE: Preparation of 3-(1-[3-(1,3-benzothiazol-6-yl)propylcarbamoyl]cycloalkyl)propanoic acid derivatives as nep inhibitors
INVENTOR(S): Hepworth, David
PATENT ASSIGNEE(S): Pfizer Inc., UK
SOURCE: U.S. Pat. Appl. Publ., 27 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004180941 | A1 | 20040916 | US 2004-800065 | 20040312 |
| AU 2004220269 | A1 | 20040923 | AU 2004-220269 | 20040309 |
| CA 2519072 | A1 | 20040923 | CA 2004-2519072 | 20040309 |
| WO 2004080985 | A1 | 20040923 | WO 2004-IB822 | 20040309 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1606272 | A1 | 20051221 | EP 2004-718706 | 20040309 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004008377 | A | 20060321 | BR 2004-8377 | 20040309 |
| CN 1761656 | A | 20060419 | CN 2004-80006939 | 20040309 |
| JP 2006526572 | T | 20061124 | JP 2006-500337 | 20040309 |
| NL 1025709 | A1 | 20040916 | NL 2004-1025709 | 20040312 |
| NL 1025709 | C2 | 20050314 | | |

| | | | | | |
|---|---|---|---|---|---|
| NO 2005004169 | A | 20051207 | NO 2005-4169 | | 20050907 |
| PRIORITY APPLN. INFO.: | | | GB 2003-5916 | A | 20030314 |
| | | | US 2003-464608P | P | 20030422 |
| | | | GB 2003-29143 | A | 20031216 |
| | | | US 2004-538079P | P | 20040120 |
| | | | WO 2004-IB822 | A | 20040309 |

OTHER SOURCE(S): MARPAT 141:277616

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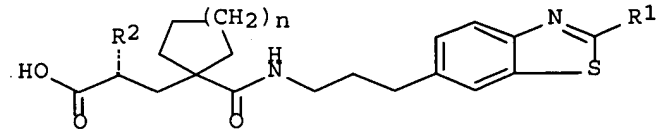

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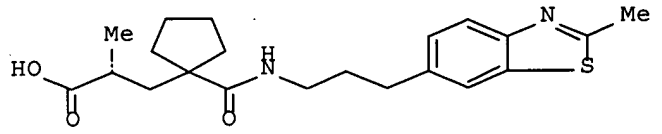


II

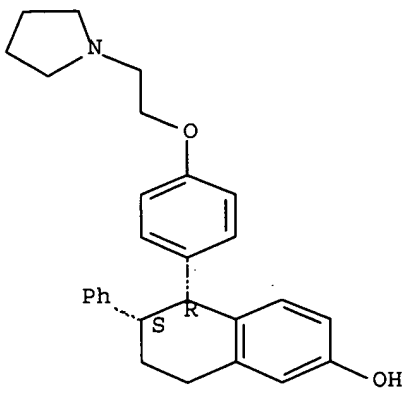
AB The invention relates to the use of title compds. I [R1 = H or Me; R2 = Me or Et; n = 1 or 2] as inhibitors of neutral endopeptidase enzyme (NEP), processes for the preparation thereof, intermediates used in the preparation thereof and compns. containing said inhibitors. Thus, e.g., II was prepared by amidation of 1-[(2R)-3-tert-butoxy-2-methyl-3-oxopropyl]cyclopentane carboxylic acid with 3-(2-methyl-1,3-benzothiazol-6-yl)propylamine dihydrochloride (preparation given) with subsequent hydrolysis to provide the free acid. I have been demonstrated to possess IC50 values of <20 nanomolar in tests for NEP inhibition and demonstrate a selectivity over soluble secreted endopeptidase (SEP) of at least 1000 fold. These inhibitors have utility in a variety of therapeutic areas including the treatment of male and female sexual dysfunction, particularly female sexual dysfunction (FSD), especially wherein the FSD is female sexual arousal disorder (FSAD).

IT 180916-16-9, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of ([(benzothiazolyl)propylcarbamoyl]cycloalkyl)propano ic acid derivs. as inhibitors of neutral endopeptidase enzyme)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:756710 HCAPLUS Full-text
DOCUMENT NUMBER: 141:277628
TITLE: Preparation of ureidophenoxycyanopyridines as anticancer drugs.
INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen; Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma, Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei; Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu, Qingming
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004078747 | A1 | 20040916 | WO 2004-US6286 | 20040301 |
| WO 2004078747 | A8 | 20041104 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004235829 | A1 | 20041125 | US 2004-788029 | 20040227 |
| AU 2004217977 | A1 | 20040916 | AU 2004-217977 | 20040301 |
| CA 2517361 | A1 | 20040916 | CA 2004-2517361 | 20040301 |
| US 2004229937 | A1 | 20041118 | US 2004-789446 | 20040301 |
| US 2005032798 | A1 | 20050210 | US 2004-788405 | 20040301 |
| US 2005038031 | A1 | 20050217 | US 2004-788426 | 20040301 |
| EP 1599467 | A1 | 20051130 | EP 2004-716144 | 20040301 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004007897 | A | 20060301 | BR 2004-7897 | 20040301 |

| | | | | | |
|---|---|---|---|---|---|
| JP 2006519264 | T | 20060824 | JP 2006-508977 | | 20040301 |
| CN 1839126 | A | 20060927 | CN 2004-80011547 | | 20040301 |
| PRIORITY APPLN. INFO.: | | | US 2003-450323P | P | 20030228 |
| | | | US 2003-450324P | P | 20030228 |
| | | | US 2003-450348P | P | 20030228 |
| | | | WO 2004-US6286 | A | 20040301 |

OTHER SOURCE(S): MARPAT 141:277628

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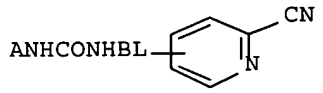


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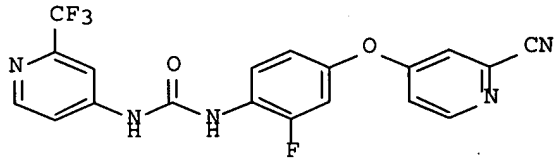



II

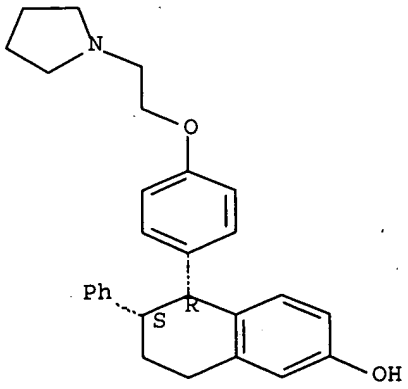
AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxy], were prepared Thus, 2-trifluoromethyl-4- pyridylamine was stirred 20 h with carbonyldiimidazole in CH2Cl2; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC50 = 7.86 nM to >1600 nM.

IT 180916-16-9, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:606368 HCAPLUS Full-text
DOCUMENT NUMBER: 141:134076
TITLE: The use of estrogen receptor alpha modulators for the treatment of multiple sclerosis
INVENTOR(S): Elloso, M. Merle; Mitchell, Robert; Harnish, Douglas C.; Adelman, Steven J.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

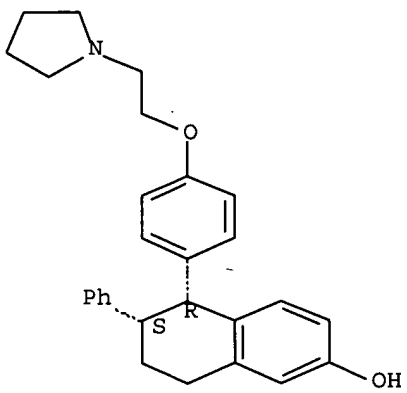
| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2004062653 | A2 | 20040729 | WO 2004-US37 | | 20040105 |
| WO 2004062653 | A3 | 20041104 | | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | | | | | |
| AU 2004204675 | A1 | 20040729 | AU 2004-204675 | | 20040105 |
| CA 2512021 | A1 | 20040729 | CA 2004-2512021 | | 20040105 |
| US 2004167112 | A1 | 20040826 | US 2004-751543 | | 20040105 |
| EP 1585507 | A2 | 20051019 | EP 2004-700191 | | 20040105 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2004006643 | A | 20051206 | BR 2004-6643 | | 20040105 |
| CN 1723013 | A | 20060118 | CN 2004-80001876 | | 20040105 |
| JP 2006515616 | T | 20060601 | JP 2006-500772 | | 20040105 |
| NO 2005003156 | A | 20050908 | NO 2005-3156 | | 20050628 |
| PRIORITY APPLN. INFO.: | | | US 2003-438123P | P | 20030106 |
| | | | WO 2004-US37 | W | 20040105 |

AB The present invention provides methods of treating an autoimmune pathol. in a mammal, comprising administering an agent with estrogen receptor-α agonist activity in particular a selective estrogen receptor modulator, to the mammal in an amount sufficient to decrease production of TH-1 and/or TH-2 cytokines. Also provided is a method of selecting compds. useful for the treatment of multiple sclerosis, comprising selecting a compound which has estrogen receptor-α agonist activity.

IT 180916-16-9, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of estrogen receptor alpha modulators for the treatment of multiple sclerosis)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:2847 HCAPLUS Full-text
DOCUMENT NUMBER: 140:71530
TITLE: Use of cyclothiocarbamate derivatives as selective androgen antagonists in contraception, hormone replacement therapy and in treatment of other hormone-related conditions
INVENTOR(S): Fensome, Andrew; Grubb, Gary; Harrison, Diane Deborah; Winneker, Richard Craig; Zhang, Puwen; Kern, Jeffrey Curtis; Terefenko, Eugene Anthony
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004000801 | A2 | 20031231 | WO 2003-US19751 | 20030623 |
| WO 2004000801 | A3 | 20040325 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2489847 | A1 | 20031231 | CA 2003-2489847 | 20030623 |
| AU 2003247608 | A1 | 20040106 | AU 2003-247608 | 20030623 |
| US 2004006060 | A1 | 20040108 | US 2003-601481 | 20030623 |
| BR 2003012024 | A | 20050322 | BR 2003-12024 | 20030623 |
| EP 1515725 | A2 | 20050323 | EP 2003-761263 | 20030623 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1662241 | A | 20050831 | CN 2003-814681 | 20030623 |

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|---|---|---|---|---|---|
| JP 2005535624 | T | 20051124 | JP 2004-516143 | | 20030623 |
| NO 2004005216 | A | 20050124 | NO 2004-5216 | | 20041129 |
| PRIORITY APPLN. INFO.: | | | US 2002-391871P | P | 20020625 |
| | | | WO 2003-US19751 | W | 20030623 |

OTHER SOURCE(S): MARPAT 140:71530

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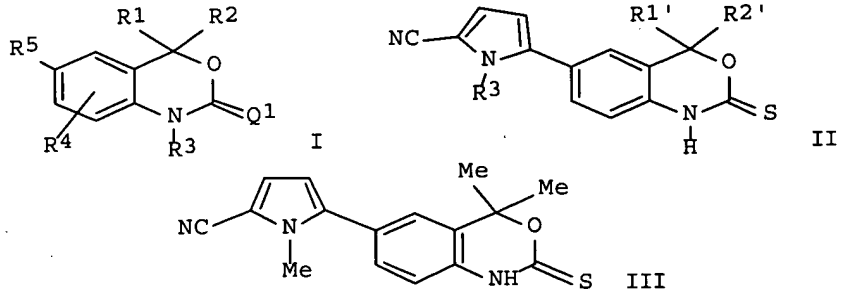


I II



III

AB The present invention provides methods of inducing contraception which includes delivering to a female a composition containing cyclothiocarbamates (shown as I and II; variables defined below; e.g. III) or tautomers thereof, in a regimen which involves delivering ≥1 of a selective estrogen receptor modulator. Methods of providing hormone replacement therapy and for treating carcinomas, dysfunctional bleeding, uterine leiomyomata, endometriosis, and polycystic ovary syndrome is provided which includes delivering I or II and a selective estrogen receptor modulator are also described. III (5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6- yl)-1-methyl-1H-pyrrole-2-carbonitrile) showed significant antagonistic activity towards androgens in L929 cells over a nine point dose response (IC50 = 109 nM) and only marginal agonistic activity at the maximum concentration tested (i.e., 10 nM). Although neither I nor II nor the methods of preparation are claimed, 6 example prepns. are included. For example, 1-methyl-5-[2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6- yl]-1H-pyrrole-2-carbonitrile was prepared in 5 steps (32, 58, 52, 79, and 49 % yields, resp.) starting from phenylcarbamic acid tert-Bu ester, cyclobutanone and tBuLi in Et2O and involving intermediates tert-Bu [2-(1-hydroxycyclobutyl)phenyl]carbamate, spiro[3,1-benzoxazine-4,1'- cyclobutan]-2(1H)-one, 6-bromospiro[3,1-benzoxazine-4,1'-cyclobutan]-2(1H)- one, and 1-methyl-5-[2-oxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'- cyclobutan]-6-yl]-1H-pyrrole-2-carbonitrile. For I: R1 and R2 = H, (un)substituted C1 to C6 alkyl, (un)substituted C2-C6 alkenyl, (un)substituted C2-C6 alkynyl, (un)substituted C3-C8 cycloalkyl, (un)substituted aryl, (un)substituted C-based heterocyclic ring having in its backbone 1-3 heteroatoms, CORA, and NRBCORA; or R1 and R2 are fused to form a ring (a), (b) and (c), wherein said ring is (un)substituted by 1-3 substituents H and C1 to C3 alkyl ((a) a C-based 3 to 8 membered saturated spirocyclic ring; (b) a C-based 3 to 8 membered spirocyclic ring having ≥1 C-C double bonds; and (c) a 3 to 8 membered spirocyclic ring having in its backbone 1-3 heteroatoms O, S and N). R3 = H, OH, NH2, (un)substituted C1 to C6 alkyl, (un)substituted C3-C6 alkenyl, (un)substituted alkynyl, and CORC; R4 = H, halogen, CN, NO2, (un)substituted C1 to C6 alkyl, C1 to C6 alkoxy, C1 to C6 aminoalkyl; R5 = an X/Y/Z-substituted Ph or a five or six membered C-based heterocyclic ring having in its backbone 1-3 heteroatoms O, S, SO, SO2, and NR6 and having one or two independent

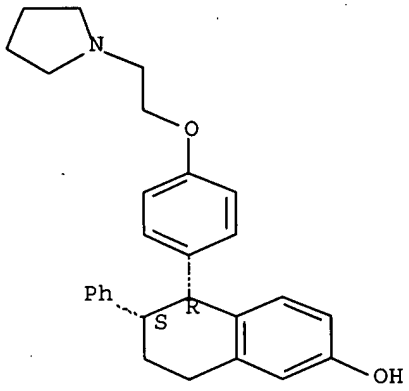
substituents H, halogen, CN, NO2, (un)substituted C1 to C4 alkyl, (un)substituted C1 to C3 alkoxy, (un)substituted C1 to C3 aminoalkyl, (un)substituted C1 to C3 perfluoroalkyl, (un)substituted 5 or 6 membered C-based heterocyclic ring having in its backbone 1-3 heteroatoms, (un)substituted C1 to C3 thioalkyl, CORF, and NRGCORF; Q1 = S, NR7, and CR8R9; addnl. details are given in the claims. For II: R1' = Me, Et, trifluoromethyl; R2' = Me, Et, trifluoromethyl; or R1' and R2' are joined to form a spirocyclic ring containing 3 to 7 C atoms; and R3 =C1 to C4 alkyl; other variables are as for I.

IT 180916-16-9, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulator as codrug; use of cyclothiocarbamate derivs. as selective androgen antagonists in contraception, hormone replacement therapy and in treatment of other hormone-related conditions)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:239231 HCAPLUS Full-text

DOCUMENT NUMBER: 139:143104

TITLE: Novel therapies for osteoporosis

AUTHOR(S): Biskobing, Diane M.

CORPORATE SOURCE: Virginia Commonwealth University/Medical College of Virginia, Richmond, VA, USA

SOURCE: Expert Opinion on Investigational Drugs (2003), 12(4), 611-621
CODEN: EOIDER; ISSN: 1354-3784

PUBLISHER: Ashley Publications Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Osteoporosis remains a significant clin. problem despite effective therapies. Many patients cannot or will not take currently available therapies. For this reason, research continues in search of more effective and more tolerable agents. Anabolic agents offer an unique mechanism of action. The anabolic agents parathyroid hormone and strontium are discussed. The investigational bisphosphonates Ibandronate, Minodronate, and Zoledronic

acid may offer the advantage of less frequent dosing. Arzoxifene, Bazedoxifene, Lasofoxifene, MDL-103,323, and Ospemifene are investigational selective estrogen receptor modulators shown to be effective in animal studies and are now in clin. studies. Tibolone is a tissue-specific steroid that is currently used in Europe for the prevention and treatment of osteoporosis. Multiple studies have shown efficacy in improving bone mineral d., but no fracture studies have been conducted to date. While studies of the effect of isoflavones on bone mineral d. have been encouraging, a large, multicenter study in Europe showed no effect of isoflavones on fractures. The newly described agent Osteoprotegerin has been shown in early studies to inhibit bone turnover. Other agents with unique mechanisms of action in early development include cathepsin K inhibitors, integrin receptor inhibitors, nitrosylated nonsteroidal anti-inflammatory agents, and Src inhibitors. The efficacy of statins in bone continues to be debated with no prospective, randomized studies yet to confirm the suggestion of benefit seen in epidemiol. studies.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:391522 HCAPLUS Full-text
DOCUMENT NUMBER: 136:395983
TITLE: Bombesin receptor antagonists, and combinations with other agents, for the treatment of sexual dysfunction
INVENTOR(S): Gonzalez, Maria Isabel; Stock, Herman Thijs; Pinnock, Robert Denham; Pritchard, Martyn Clive; Wayman, Christopher Peter; Van der Graaf, Pieter Hadewijn; Naylor, Alisdair Mark; Higginbottom, Michael
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002040008 | A2 | 20020523 | WO 2001-GB5018 | 20011114 |
| WO 2002040008 | A3 | 20020822 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| WO 2002040022 | A1 | 20020523 | WO 2000-GB4380 | 20001117 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, | | | | |

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| CA 2429106 | A1 | 20020523 | CA 2001-2429106 | | 20011114 |
| AU 200223802 | A | 20020527 | AU 2002-23802 | | 20011114 |
| EP 1333824 | A2 | 20030813 | EP 2001-994552 | | 20011114 |
| EP 1333824 | B1 | 20050907 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| BR 2001015364 | A | 20030923 | BR 2001-15364 | | 20011114 |
| HU 200301892 | A2 | 20031128 | HU 2003-1892 | | 20011114 |
| JP 2004522710 | T | 20040729 | JP 2002-542382 | | 20011114 |
| NZ 525415 | A | 20041126 | NZ 2001-525415 | | 20011114 |
| AT 303804 | T | 20050915 | AT 2001-994552 | | 20011114 |
| US 2004087561 | A1 | 20040506 | US 2003-416934 | | 20031204 |
| PRIORITY APPLN. INFO.: | | | WO 2000-GB4380 | W | 20001117 |
| | | | GB 2001-9910 | A | 20010423 |
| | | | GB 2001-11037 | A | 20010504 |
| | | | WO 2001-GB5018 | W | 20011114 |

OTHER SOURCE(S): MARPAT 136:395983

AB Bombesin receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of bombesin receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Preparation of compds. of the invention is described.

L8 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:314394 HCAPLUS Full-text

DOCUMENT NUMBER: 136:335264

TITLE: Use of an estrogen agonists and antagonists for assessment, improvement, or maintenance of urogenital health

INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1199069 | A2 | 20020424 | EP 2001-308625 | 20011009 |
| EP 1199069 | A3 | 20031119 | | |
| EP 1199069 | B1 | 20061004 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| AT 341313 | T | 20061015 | AT 2001-308625 | 20011009 |
| CA 2358938 | A1 | 20020416 | CA 2001-2358938 | 20011012 |
| CA 2358938 | C | 20060808 | | |
| CA 2541348 | A1 | 20020416 | CA 2001-2541348 | 20011012 |
| US 2002128276 | A1 | 20020912 | US 2001-976825 | 20011012 |
| JP 2002179593 | A | 20020626 | JP 2001-316248 | 20011015 |
| HU 200104300 | A2 | 20020828 | HU 2001-4300 | 20011015 |
| ZA 2001008443 | A | 20030415 | ZA 2001-8443 | 20011015 |
| NZ 514821 | A | 20040130 | NZ 2001-514821 | 20011015 |

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|---|---|---|---|---|---|
| AU 783821 | B2 | 20051208 | AU 2001-79412 | | 20011015 |
| US 2003125319 | A1 | 20030703 | US 2002-292203 | | 20021112 |
| US 2005215592 | A1 | 20050929 | US 2005-137830 | | 20050524 |
| PRIORITY APPLN. INFO.: | | | US 2000-240789P | P | 20001016 |
| | | | CA 2001-2358938 | A3 | 20011012 |
| | | | US 2001-976825 | A3 | 20011012 |
| | | | US 2002-292203 | A1 | 20021112 |

OTHER SOURCE(S): MARPAT 136:335264

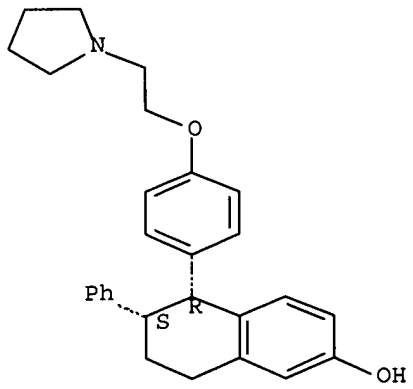
AB The invention relates to methods and kits useful for the improvement, or maintenance urogenital health using an estrogen agonist/antagonist compds. (Markush structures are included). The methods of treatment are effective for improving or maintaining urogenital health while substantially reducing the concomitant liability of adverse effects associated with estrogen administration. This invention also relates to methods of assessing vaginal health.

IT 180916-16-9
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of estrogen agonists and antagonists for assessment, improvement, or maintenance of urogenital health)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2001:762983 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 135:303769 |
| TITLE: | Preparation of estrogen agonist/antagonist metabolites |
| INVENTOR(S): | Day, Wesley Warren; Johnson, Kim Anne; Prakash, Chandra Aggarwal; Eggler, James Frederick |
| PATENT ASSIGNEE(S): | Pfizer Products Inc., USA |
| SOURCE: | PCT Int. Appl., 80 pp. CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2001077093 | A1 | 20011018 | WO 2001-IB427 | | 20010319 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2405070 | A1 | 20011018 | CA 2001-2405070 | | 20010319 |
| EP 1268453 | A1 | 20030102 | EP 2001-912069 | | 20010319 |
| EP 1268453 | B1 | 20060719 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| BR 2001009838 | A | 20030121 | BR 2001-9838 | | 20010319 |
| HU 200300419 | A2 | 20030628 | HU 2003-419 | | 20010319 |
| NZ 521291 | A | 20040227 | NZ 2001-521291 | | 20010319 |
| JP 2004510693 | T | 20040408 | JP 2001-575567 | | 20010319 |
| EE 200200580 | A | 20040615 | EE 2002-580 | | 20010319 |
| AT 333450 | T | 20060815 | AT 2001-912069 | | 20010319 |
| US 2002042443 | A1 | 20020411 | US 2001-825980 | | 20010404 |
| US 6455572 | B2 | 20020924 | | | |
| IN 2002DN00888 | A | 20050121 | IN 2002-DN888 | | 20020912 |
| BG 107137 | A | 20030530 | BG 2002-107137 | | 20020923 |
| NO 2002004767 | A | 20021203 | NO 2002-4767 | | 20021003 |
| ZA 2002007995 | A | 20031020 | ZA 2002-7995 | | 20021004 |
| US 39419 | E1 | 20061205 | US 2003-448751 | | 20030530 |
| HK 1052511 | A1 | 20050930 | HK 2003-104866 | | 20030708 |
| PRIORITY APPLN. INFO.: | | | US 2000-267198P | P | 20000407 |
| | | | WO 2001-IB427 | W | 20010319 |
| | | | US 2001-825980 | E | 20010404 |

OTHER SOURCE(S): MARPAT 135:303769

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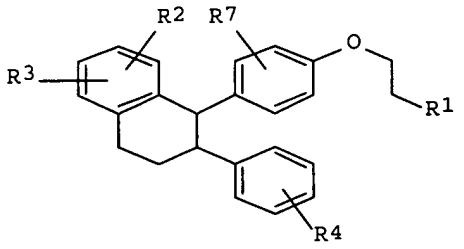



I

AB This invention relates to compds. represented by formula [I; R1 = pyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 2-hydroxy-1-pyrrolidin-1-yl, 2-methoxy-1-pyrrolidin-1-yl, NH(CH2)3COR6 (where R6 = OH, NHCH2CO2H); R2, R3, R4, R7 = H, OH, OMe; provided that (a) if R1 is pyrrolidin-1-yl or NH(CH2)3CO2H, and (b) R2 is OH or OMe and R3 and R7 are H, or if R1 is defined in (a) and (c) R2 and R7 are H and R3 is OH or OMe, then R4 is not H] which are mammalian metabolites of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin- 1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol (PPTN) and are believed to possess

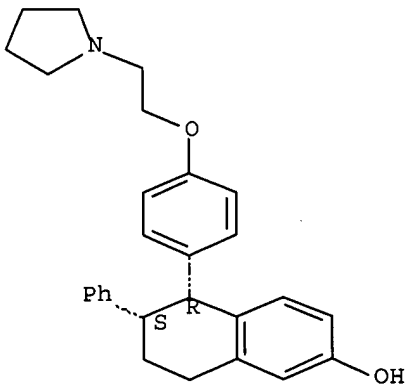
significant pharmacol. activities similar or identical to those possessed by the parent PPTN. The compds. of the invention can be used as stds. for anal. assays or as intermediates for the further chemical synthesis or biosynthesis of chemical entities. The invention also relates to pharmaceutical compns. for the treatment of disease and methods of treating disease. Examples of diseases or conditions for which the compds. can be effective include osteoporosis, breast cancer, hyperlipidemia, atherosclerosis, Alzheimer's disease, cataracts, loss of libido, male sexual dysfunction, colon cancer, skin wrinkles, autoimmune disease, alopecia, acne, cardiovascular disease, cataracts, diabetes, endometriosis, female sexual dysfunction, hyperglycemia, obesity, obsessive compulsive disorder, etc. (no data). Thus, 1-[2-[4-(2-Bromo-6,7- dimethoxy-3,4-dihydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine was coupled with phenylboronic acid in the presence of tetrakis(triphenylphosphine)pal ladium and Na2CO3 in EtOH at room temperature for 10 h to give 1-[2-[4-(6,7-dimethoxy-2-phenyl-3,4-dihydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine which was hydrogenated Pd(OH)2 on carbon in a mixture of 2 N aqueous HCl, H2O, and EtOH at 50° under a H atmospheric of 30 psi to give 1-[2-[4-(6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine. The latter compound was heated in a mixture of AcOH and 48% aqueous HBr at 90° for 2 h to give cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2,3-diol and a mixture of cis-3-methoxy-7-phenyl-8-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol and cis-3-methoxy-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol.

IT 180916-16-9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(animal metabolism; preparation of metabolites of (-)-cis-phenyl[(pyrrolidinylethoxy)phenyl]tetrahydronaphthalenol estrogen agonist/antagonist as therapeutic agents)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:559558 HCAPLUS Full-text

DOCUMENT NUMBER: 135:142234
TITLE: Compositions and methods for treating conditions responsive to estrogen
INVENTOR(S): Thompson, David Duane; Lee, Andrew George; Day, Wesley Warren; Rosati, Robert Louis
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1120114 | A2 | 20010801 | EP 2001-300221 | 20010111 |
| EP 1120114 | A3 | 20030820 | | |
| EP 1120114 | B1 | 20061122 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR | | | | |
| ZA 2001000177 | A | 20020708 | ZA 2001-177 | 20010108 |
| TW 246918 | B | 20060111 | TW 2001-90100370 | 20010108 |
| CA 2331053 | A1 | 20010712 | CA 2001-2331053 | 20010110 |
| CA 2331053 | C | 20051025 | | |
| CA 2475393 | A1 | 20010712 | CA 2001-2475393 | 20010110 |
| US 2001041718 | A1 | 20011115 | US 2001-758778 | 20010111 |
| US 6632834 | B2 | 20031014 | | |
| NZ 509321 | A | 20021025 | NZ 2001-509321 | 20010111 |
| HU 200100120 | A2 | 20021028 | HU 2001-120 | 20010111 |
| AU 780142 | B2 | 20050303 | AU 2001-13676 | 20010111 |
| AT 345794 | T | 20061215 | AT 2001-300221 | 20010111 |
| JP 2001213776 | A | 20010807 | JP 2001-4452 | 20010112 |
| US 2004092506 | A1 | 20040513 | US 2003-652186 | 20030829 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2000-175752P | P | 20000112 |
| CA 2001-2331053 | A3 | 20010110 |
| US 2001-758778 | A3 | 20010111 |

OTHER SOURCE(S): MARPAT 135:142234

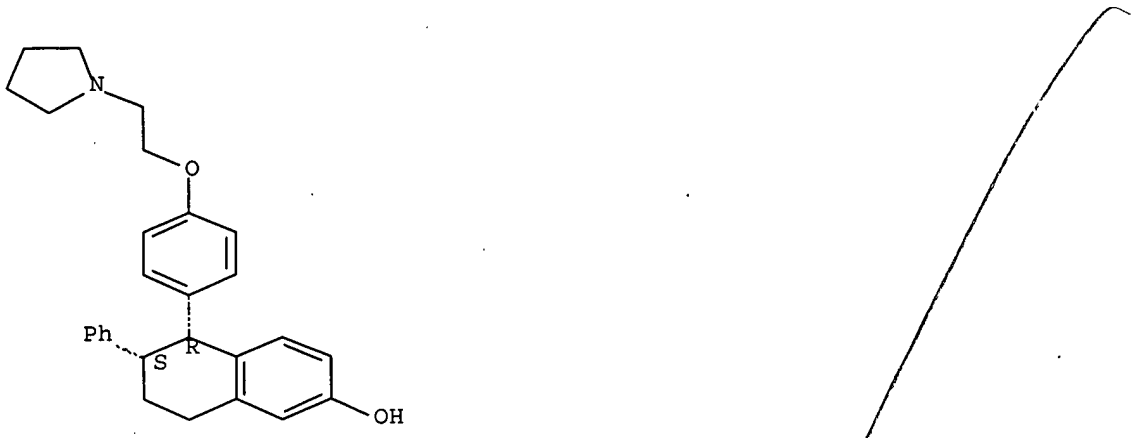
AB This invention relates to methods, pharmaceutical compns. and kits useful in treating conditions responsive to estrogen by the administration of estrogen agonists/antagonists. Conditions responsive to the compns. include rheumatoid arthritis, colon cancer, tissue wounds, skin wrinkles and cataracts. The compns. are comprised of an estrogen agonist/antagonist and a pharmaceutically acceptable vehicle, carrier or diluent. The compns. and methods of treatment are effective while substantially reducing the concomitant liability of adverse effects associated with estrogen administration. The in vitro antiproliferative effects of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8- tetrahydronaphthalene-2-ol were tested in 2 types of human breast cancer cell lines: first, MCF-7 cells, which contain ER as well as progesterone receptors (PgR), and second, MDA-MB-231 cells, which lack ER and PgR, and enable the determination of an effect that is independent of the ER mechanism. Growth inhibition was ER-specific and not due to cytotoxicity since the compound had no measurable effect on the ER-neg. cell line.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for treating conditions responsive to estrogen)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L8 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:450913 HCAPLUS Full-text

DOCUMENT NUMBER: 129:184100

TITLE: Discovery and Preclinical Pharmacology of a Novel, Potent, Nonsteroidal Estrogen Receptor Agonist/Antagonist, CP-336156, a Diaryltetrahydronaphthalene

AUTHOR(S): Rosati, Robert L.; Jardine, Paul Da Silva; Cameron, Kimberly O.; Thompson, David D.; Ke, Hua Zhu; Toler, Steven M.; Brown, Thomas A.; Pan, Lydia C.; Ebbinghaus, Charles F.; Reinhold, Anthony R.; Elliott, Nancy C.; Newhouse, Bradley N.; Tjoa, Christina M.; Sweetnam, Paul M.; Cole, Mark J.; Arriola, Mark W.; Gauthier, Jeffrey W.; Crawford, D. Todd; Nickerson, David F.; Pirie, Christine M.; Qi, Hong; Simmons, Hollis A.; Tkalcevic, George T.

CORPORATE SOURCE: Central Research Division, Pfizer Inc., Groton, CT, 06340, USA

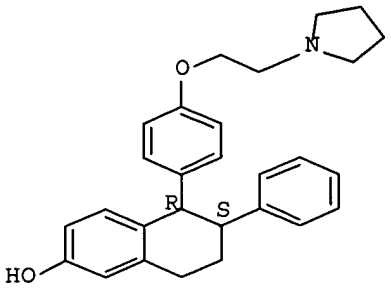
SOURCE: Journal of Medicinal Chemistry (1998), 41(16), 2928-2931
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

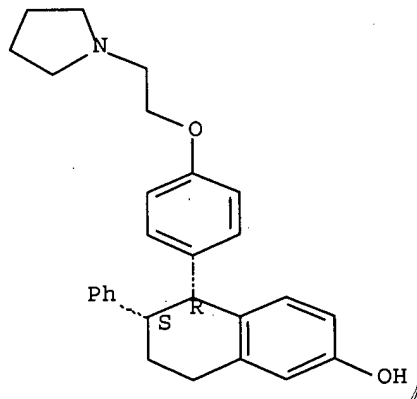
AB CP-336156 (I), a nonsteroidal estrogen agonist/antagonist with excellent oral bioavailability, was prepared and is as potent and efficacious as estrogen at preventing bone loss and lowering total serum cholesterol in rats. In addition, estrogen-like proliferative effects on breast and uterine tissue were not observed The superior oral kinetics, achieved by minimizing intestinal glucuronidation through the application of a structural model, translated into a breakthrough for in vivo potency.

IT 180916-16-9P, 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2 SEL PLU=ON L1 1- CHEM : 2 TERMS

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L5       260272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("INFLAMMATORY BOWEL DISEASE"/
                CV OR "INTESTINE, DISEASE (L) INFLAMMATORY"/CV) OR BOWEL OR
                INTESTIN?
L6           16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L5
L7            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(L)?INFLAMM?
L8           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 OR L7
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                BURTON"/AU) OR MACLEAN D/AU OR MACLEAN D B/AU
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L15          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L12 OR L13) AND L3
L16          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L12 OR L13) AND L5
L17          49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 OR L15 OR L16
L18          46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 NOT L8


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=> d ibib abs hitstr l18 1-46

L18  ANSWER 1 OF 46  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:1156816  HCAPLUS  Full-text
DOCUMENT NUMBER:          145:465947
TITLE:                    Pharmaceutical compositions and methods comprising a
                          combination of a selective estrogen receptor modulator
                          and an aromatase inhibitor
INVENTOR(S):              Curto, Madelyn; Sisson, Melanie; Lee, Andrew George;
                          Thompson, David Duane
PATENT ASSIGNEE(S):       Pfizer Products Inc., USA
SOURCE:                   PCT Int. Appl., 29pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    -------------------    --------
     WO 2006114702         A2    20061102    WO 2006-IB1040         20060413
     WO 2006114702         A3    20070104
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
```

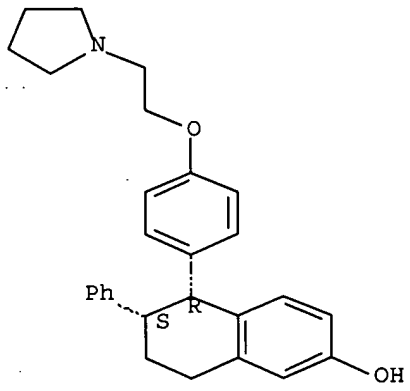
JP 2006306872 A 20061109 JP 2006-118713 20060424
PRIORITY APPLN. INFO.: US 2005-674807P P 20050425

AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-(-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)- phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol or a pharmaceutically acceptable salt or prodrug thereof and an aromatase inhibitor. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8- tetrahydronaphthalene-2-ol or a pharmaceutically acceptable salt or prodrug and an aromatase inhibitor selected from aminoglutethimide; formestane; atamestane; anastrazole; fadrozole; finrozole; letrozole; vorozole; 4-[N-(4-bromobenzyl)-N-(4-cyanophenyl)amino]-4H-1 ,2,4-triazole or exemestane, or a pharmaceutically acceptable salt thereof.

IT 180916-16-9
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. and methods comprising a combination of a selective estrogen receptor modulator and an aromatase inhibitor)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1019408 HCAPLUS Full-text
DOCUMENT NUMBER: 146:75472
TITLE: Effect of glucagon-like peptide-1 (7-37) on beta-cell function after islet transplantation in type 1 diabetes
AUTHOR(S): Fung, Michelle; Thompson, David; Shapiro, R. Jean; Warnock, Garth L.; Andersen, Dana K.; Elahi, Dariush; Meneilly, Graydon S.
CORPORATE SOURCE: Department of Medicine, University of British Columbia, Vancouver, BC, Can.
SOURCE: Diabetes Research and Clinical Practice (2006), 74(2), 189-193

CODEN: DRCPE9; ISSN: 0168-8227
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Islet transplantation can improve glycemic control in patients with type 1 diabetes and reduce or eliminate the need for insulin. Glucagon-like peptide-1 (GLP-1) is an intestinal insulinotropic hormone that augments glucose induced insulin secretion, and has a trophic effect on beta-cells. We evaluated the effect of GLP-1 on insulin secretion after islet transplantation. Patients underwent hyperglycemic glucose clamp studies 1 mo after their last transplant. GLP-1 was infused during the second hour of the hyperglycemic clamp. Results were compared to normal control subjects and patients with type 2 diabetes who underwent an identical hyperglycemic clamp. First phase insulin release was absent in patients, while second phase insulin was not significantly reduced (control: 118 ± 29 pM; type 2 diabetes: 68 ± 20 pM; transplant: 99 ± 18 pM, p = ns for all). GLP-1 had a significant incretin effect on transplanted islets but the response was less than controls (control: 2108 ± 344 pM; type 2 diabetes: 929 ± 331 pM; transplant: 329 ± 112 pM, p < 0.0001 control vs. transplant). Islet transplant patients had no evidence of resistance to insulin mediated glucose disposal. We conclude that transplanted islets retain the ability to respond to GLP-1.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:878823 HCAPLUS Full-text
DOCUMENT NUMBER: 146:26080
TITLE: Expression of TECK/CCL25 and MEC/CCL28 chemokines and their respective receptors CCR9 and CCR10 in porcine mucosal tissues
AUTHOR(S): Meurens, Francois; Berri, Mustapha; Whale, Julia; Dybvig, Tova; Strom, Stacy; Thompson, David; Brownlie, Robert; Townsend, Hugh G. G.; Salmon, Henri; Gerdts, Volker
CORPORATE SOURCE: Vaccine and Infectious Disease Organization, University of Saskatchewan, Saskatoon, SK, S7N 5E3, Can.
SOURCE: Veterinary Immunology and Immunopathology (2006), 113(3-4), 313-327
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CCL25 and CCL28 (also named TECK and MEC) are CC chemokines primarily expressed by thymic dendritic cells and mucosal epithelial cells. The cognate receptors of CCL25 and CCL28, named CCR9 and CCR10, are mainly expressed on T lymphocytes for CCR9 and IgA+ and IgM+ plasmablasts for CCR9 and CCR10, resp. In human and mouse, chemokines CCL25 and CCL28 play an important role in attracting immune cells to the gastrointestinal tract and in controlling segmental specialization of the intestinal immune system. To investigate if CCL25 and CCL28 play a similar role in the pig and to better understand lymphocyte trafficking in this species, the authors cloned porcine CCL25 and CCR10 and measured expression of CCL25, CCL28, CCR9, and CCR10 transcripts by real-time and conventional PCR in various tissues from newborn and young piglets, and adult sows. The results of the expression analyses show that (1) expression of CCL25 mRNA is mainly restricted to the small intestine, (2) CCL28 mRNA expression is detectable in all tested epithelial mucosal surfaces with the highest levels of expression in the mammary gland, trachea and large

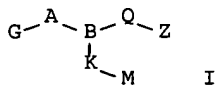
intestine, (3) high levels of expression of CCR9 mRNA in CD3+ T lymphocytes, gut-associated lymphoid tissues (GALT), and the small intestine, (4) high levels of expression of CCR10 mRNA in GALT, the large intestine, the small intestine, and the mammary gland, and (5) up-regulation of CCL28 mRNA expression during lactation in the mammary gland. This pattern of expression, which is discussed in the context of compartmentalization of the porcine common mucosal immune system into upper aero-digestive tract, small intestine, and large intestine, suggests a key role for CCL28 in the recruitment of IgA secreting cells into the mammary gland enabling the passive transfer of IgA antibodies from mother to infant.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1004350 HCAPLUS Full-text
DOCUMENT NUMBER: 143:306176
TITLE: Preparation of heterocyclic compounds as EP2 selective receptor agonists for treating pulmonary hypertension and other conditions
INVENTOR(S): Constan, Alexander A.; Keshary, Prakash; MacLean, David B.; Paralkar, Vishwas M.; Roman, Doina; Thompson, David D.; Wright, Timothy M.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 82 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005203086 | A1 | 20050915 | US 2004-793530 | 20040304 |
| PRIORITY APPLN. INFO.: | | | US 2004-793530 | 20040304 |

OTHER SOURCE(S): MARPAT 143:306176
GI




I

AB The present invention relates to methods of treating pulmonary hypertension, facilitating joint fusion, facilitating tendon and ligament repair, reducing the occurrence of secondary fracture, treating avascular necrosis, facilitating cartilage repair, facilitating bone healing after limb transplantation, facilitating liver regeneration, facilitating wound healing, reducing the occurrence of gastric ulceration, treating hypertension, facilitating the growth of tooth enamel or finger or toe nails, treating glaucoma, treating ocular hypertension, and repairing damage caused by metastatic bone disease using the compds. I [A = SO2, CO; G = Ar, Ar(alkylene), ArCONH(alkylene), etc.; B = N, CH; Q = alkylene, X(alkylene), X(alkylene), etc.; Z = carboxy, alkoxycarbonyl, tetrazolyl, etc.; K = a bond,

alkylene, thioalkylene, etc.; M = Ar3, Ar4SAr5, Ar4OAr5, etc.; Ar, Ar3-Ar5 = partially saturated or fully unsatd. 5-8 membered ring having 1-4 heteroatoms selected from O, S, N, or a bicyclic ring, tricycling ring, etc.; X = X = 5-6 membered aromatic ring optionally having 1-2 heteroatoms selected from O, N and S], an EP2 selective receptor agonists. Syntheses of representative compds. I and their intermediates are described in several examples. E.g., a 3-step synthesis of 7-[(4-butylbenzyl)-(pyridine-3-sulfonyl)amino]heptanoic acid, starting from Me 7-aminoheptanoate (preparation given) and 4-butylbenzaldehyde, was given. The compds. I were tested for binding to prostaglandin E2 receptors (data given for exemplified compds. I).

L18 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259665 HCAPLUS Full-text
DOCUMENT NUMBER: 142:310360
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of anorexia or low bone mass in females exhibiting aggressive athletic behavior
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005065134 | A1 | 20050324 | US 2004-944368 | 20040916 |
| WO 2005027925 | A1 | 20050331 | WO 2004-IB2904 | 20040906 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504510P P 20030919
OTHER SOURCE(S): CASREACT 142:310360
AB The present invention relates to methods of treating anorexia or low bone mass in females exhibiting aggressive athletic behavior, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating anorexia or low bone mass in females exhibiting aggressive athletic behavior, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)- 1α,25-dihydroxy-vitamin D3.

L18 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259663 HCAPLUS Full-text
DOCUMENT NUMBER: 142:310359
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D

derivatives for the treatment or prevention of a second hip fracture
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 2005065132 | A1 | 20050324 | US 2004-944065 | 20040916 |
| WO 2005027919 | A1 | 20050331 | WO 2004-IB2914 | 20040906 |

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PRIORITY APPLN. INFO.: US 2003-504004P P 20030919
OTHER SOURCE(S): CASREACT 142:310359

AB The present invention relates to methods of treating or preventing a second hip fracture, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating or preventing a second hip fracture, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)- 1α,25-dihydroxyvitamin D 3.

L18 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259662 HCAPLUS Full-text
DOCUMENT NUMBER: 142:310358
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for enhancement of peak bone mass in adolescence
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 2005065131 | A1 | 20050324 | US 2004-944063 | 20040916 |
| WO 2005027927 | A1 | 20050331 | WO 2004-IB2906 | 20040906 |

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SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504511P P 20030919
OTHER SOURCE(S): CASREACT 142:310358

AB The present invention relates to methods of enhancing peak bone mass in adolescence, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of enhancing peak bone mass in adolescence, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3.

L18 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1050178 HCAPLUS Full-text
DOCUMENT NUMBER: 142:253438
TITLE: Lasofoxifene, a next generation estrogen receptor modulator: preclinical studies
AUTHOR(S): Maeda, Tomoko; Ke, Hua Zhu; Simmons, Hollis; Thompson, David
CORPORATE SOURCE: Tokyo Laboratories, Clinical Research, Pfizer Japan Inc. Pfizer Global Research and Development, Japan
SOURCE: Clinical Calcium (2004), 14(10), 1555-1563
CODEN: CLCCEJ; ISSN: 0917-5857
PUBLISHER: Iyaku Janarusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

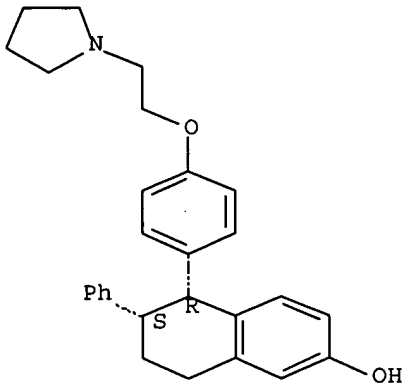
AB A review. Estrogen replacement therapy, in spite of efficacy in the prevention of osteoporotic fractures, has significant side effects and risks that limit its widespread usage in postmenopausal women. Thus significant medical need exists to find modalities that prevent osteoporosis, but without the side effects of estrogen. Selective estrogen receptor modulators (SERMs) have the potential to provide the skeletal benefits of estrogen without the increased risk of uterine and breast cancer. Tamoxifen, a first generation SERM is approved for the prevention and treatment of breast cancer, and raloxifene, a second generation SERM has been approved for the prevention and treatment of osteoporosis. Lasofoxifene, a new potent, nonsteroidal SERM, binds with high affinity to human estrogen receptors and acts as a tissue selective estrogen antagonist or agonist. In preclin. models of postmenopausal osteoporosis, lasofoxifene inhibited bone turnover and prevented bone loss throughout the skeleton. In studies designed to investigate the combination of lasofoxifene with estrogen, lasofoxifene blocked the hypertrophic effects of estrogen in the uterus, but did not block the bone protective effects. In immature and aged female rats, lasofoxifene did not affect the uterine weight and uterine histol. In preclin. studies designed to evaluate the effects of lasofoxifene on the uterus, a slight increase in wet uterine weight was observed in immature and aged female rats, but this difference was not observed in dry uterine weight suggesting that the increased uterine weight was due to increased water content in the tissue. In preclin. studies designed to evaluate the effects of lasofoxifene in breast cancer, lasofoxifene inhibited breast tumor formation in mice injected with

human MCF-7 breast cancer cells and in rats bearing mammary carcinomas. Thus, in preclin. models, lasofoxifene, a next generation SERM, prevents estrogen deficiency-induced bone loss, inhibits breast tumor formation, and reduces serum cholesterol, without causing uterine hypertrophy. These data suggest that lasofoxifene is a new potential therapy for the prevention of osteoporosis in postmenopausal women.

IT 180916-16-9, Lasofoxifene
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene, a next generation estrogen receptor modulator for treatment of postmenopausal osteoporosis)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:754428 HCAPLUS Full-text
DOCUMENT NUMBER: 141:254616
TITLE: Use of EP2 selective receptor agonists in medical treatment of pulmonary hypertension and other conditions
INVENTOR(S): Constan, Alexander Angelo; Keshary, Prakash Raj; MacLean, David Burton; Paralkar, Vishwas Madhav; Roman, Doina Cosma; Thompson, David Duane; Wright, Timothy Michael
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004078169 | A1 | 20040916 | WO 2004-IB553 | 20040223 |
| WO 2004078169 | A8 | 20050421 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 2004216898 | A1 | 20040916 | AU 2004-216898 | 20040223 |
| CA 2518193 | A1 | 20040916 | CA 2004-2518193 | 20040223 |
| EP 1601351 | A1 | 20051207 | EP 2004-713611 | 20040223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2004008061 | A | 20060214 | BR 2004-8061 | 20040223 |
| JP 2006519250 | T | 20060824 | JP 2006-506276 | 20040223 |
| CN 1859903 | A | 20061108 | CN 2004-80008576 | 20040223 |
| PRIORITY APPLN. INFO.: | | | US 2003-451889P P | 20030304 |
| | | | WO 2004-IB553 A | 20040223 |

OTHER SOURCE(S): MARPAT 141:254616

AB The invention discloses methods for treating pulmonary hypertension, facilitating joint fusion, facilitating tendon and ligament repair, reducing the occurrence of secondary fracture, treating avascular necrosis, facilitating cartilage repair, facilitating bone healing after limb transplantation, facilitating liver regeneration, facilitating wound healing, reducing the occurrence of gastric ulceration, treating hypertension, facilitating the growth of tooth enamel or finger or toe nails, treating glaucoma, treating ocular hypertension, and repairing damage caused by metastatic bone disease using an EP2 selective receptor agonist. Preparation of compds., e.g. 7-[(4-butylbenzyl)-(pyridine-3- sulfonyl)amino]heptanoic acid, is described.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:260137 HCAPLUS Full-text
DOCUMENT NUMBER: 140:350501
TITLE: Long-term treatment of lasofoxifene preserves bone mass and bone strength and does not adversely affect the uterus in ovariectomized rats
AUTHOR(S): Ke, Hua Zhu; Foley, George L.; Simmons, Hollis A.; Shen, Victor; Thompson, David D.
CORPORATE SOURCE: Pfizer Global Research and Development, Groton Laboratories, Groton, CT, 06340, USA
SOURCE: Endocrinology (2004), 145(4), 1996-2005
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to determine the long-term effects of lasofoxifene, a new selective estrogen receptor modulator, on bone mass, bone strength, and reproductive tissues in ovariectomized (OVX) rats. Sprague Dawley female rats at 3.5 mo of age were OVX and treated orally with lasofoxifene (60, 150, or 300 μg/kg·d) for 52 wk. The urinary deoxypyridinoline/creatinine ratio was significantly lower in all lasofoxifene-treated OVX rats compared with OVX controls at wk 26. Peripheral quant. computerized tomog. anal. of proximal tibial metaphysis showed that the significant loss in trabecular content and d. induced by OVX was significantly prevented by lasofoxifene treatment. Proximal tibial and lumbar vertebral trabecular bone histomorphometric anal. showed that all doses of lasofoxifene

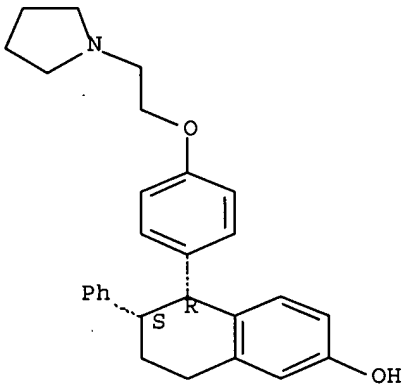
significantly reduced OVX-induced bone loss by decreasing bone resorption and bone turnover. The ultimate strength, energy, and toughness of the fourth lumbar vertebral body in OVX rats treated with all doses of lasofoxifene were significantly higher compared with those in OVX controls, and did not differ significantly from those in sham controls. Uterine weight in OVX rats treated with lasofoxifene was slightly, but significantly, higher when compared with that in OVX controls, but was still much less than that in sham controls. No abnormal finding associated with lasofoxifene was observed with uterine histol. examination In summary, long-term treatment with lasofoxifene preserves bone mass and bone strength and does not adversely affect the uterus in OVX rats. These data suggest that lasofoxifene is an effective antiosteoporosis agent, and its efficacy and safety can be maintained over an extended period of time.

IT 180916-16-9, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term treatment of lasofoxifene preserves bone mass and bone strength and does not adversely affectuterus in ovariectomized rats)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:336422 HCAPLUS Full-text

DOCUMENT NUMBER: 139:316344

TITLE: Lasofoxifene (CP-336156), a novel selective estrogen receptor modulator, in preclinical studies

AUTHOR(S): Ke, H. Z.; Brown, T. A.; Thompson, D. D.

CORPORATE SOURCE: Osteoporosis Research, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, USA

SOURCE: Journal of the American Aging Association (2002), 25(2), 87-99
CODEN: JAAABY

PUBLISHER: Journal of the American Aging Association

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

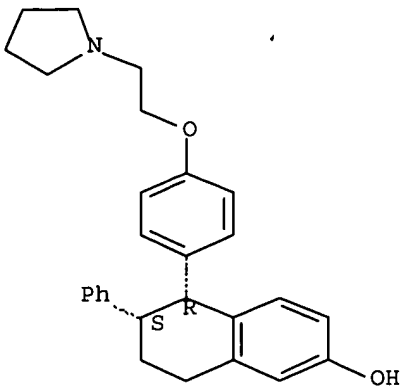
AB A review. Estrogen replacement therapy is reported to reduce the incidence of vertebral fractures in postmenopausal women, however, its compliance is limited because of side effects and safety concerns. Estrogen's side effects on breast and uterine tissues leading to the potential increased risk of uterine and breast cancer limit widespread estrogen usage. Thus, there is a significant medical need for a therapy that protects against postmenopausal bone loss but is free of estrogen's neg. effects on reproductive tissues. Selective estrogen receptor modulators (SERMs) have been investigated as an alternative to hormone replacement therapy. One such compound, raloxifene, has been approved for the prevention and treatment of osteoporosis. Lasofoxifene (LAS), a new, nonsteroidal, and potent SERM, is an estrogen antagonist or agonist depending on the target tissue. LAS selectively binds with high affinity to human estrogen receptors. In ovariectomized (OVX) rat studies, LAS prevented the decrease in femoral bone mineral d., tibial and lumbar vertebral trabecular bone mass at an ED100 of about 60 μg/kg/day. LAS inhibited the activation of trabecular and endocortical bone resorption and bone turnover in tibial metaphyses and diaphyses, and lumbar vertebral body in OVX rats. In addition, LAS decreased total serum cholesterol, inhibited body weight gain and increased soleus muscle weight in OVX rats. Similarly, LAS prevented bone loss induced by orchidectomy or aging in male rats by decreasing bone resorption and bone turnover while it had no effect in the prostate. Further, LAS decreased total serum cholesterol in intact aged male rats or in orchidectomized male rats. Synergestic skeletal effects were found with LAS in combination with bone anabolic agents such as prostaglandin E2 (PGE2), parathyroid hormone (PTH) or a growth hormone secretagogue (GHS) in OVX rats. In combination with estrogen, LAS inhibited the uterine stimulating effects of estrogen but did not block the bone protective effects of estrogen. In immature and aged female rats, LAS did not affect the uterine weight and uterine histol. In OVX adult female rats, LAS slightly but significantly increased uterine weight These results demonstrated that LAS produced effects on the skeleton indistinguishable from estrogen in female and male rats. However, unlike estrogen, LAS had little effect on uterine weight and cellular proliferation of uterus in female rats. In preclin. anti-tumor studies, LAS inhibited human breast cancer growth in mice bearing MCF7 tumors, prevented NMU-induced mammary carcinomas and possessed chemotherapeutic effects in NMU-induced carcinomas in rats. Therefore, we conclude that LAS possesses the antiestrogenic effects in breast tissue and estrogenic effects in bone and serum cholesterol, but lacks estrogen's side effects on uterine tissue. These data support the therapeutic potential of LAS for the prevention and treatment of postmenopausal bone loss and mammary carcinomas in humans.

IT 180916-16-9, Lasofoxifene
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene (CP-336156), a novel selective estrogen receptor modulator, in preclin. studies)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:117617 HCAPLUS Full-text
DOCUMENT NUMBER: 138:147771
TITLE: Pharmaceutical compositions, kits and methods comprising combinations of estrogen agonists/antagonists, estrogens and progestins
INVENTOR(S): Ke, Hua Zhu; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003011282 | A1 | 20030213 | WO 2002-IB2763 | 20020704 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2448235 | A1 | 20030213 | CA 2002-2448235 | 20020704 |
| NZ 529511 | A | 20031219 | NZ 2002-529511 | 20020704 |
| EP 1411922 | A1 | 20040428 | EP 2002-743537 | 20020704 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| HU 200401268 | A2 | 20041129 | HU 2004-1268 | 20020704 |
| JP 2005504032 | T | 20050210 | JP 2003-516512 | 20020704 |
| CN 1599606 | A | 20050323 | CN 2002-813867 | 20020704 |
| US 2003065017 | A1 | 20030403 | US 2002-206587 | 20020726 |
| US 7030157 | B2 | 20060418 | | |

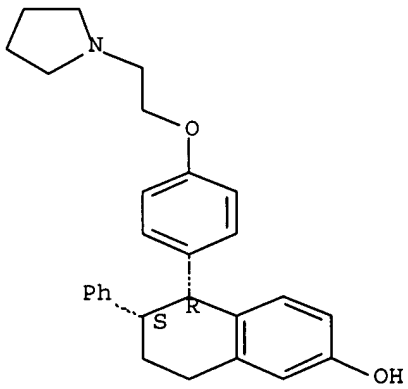
ZA 2003008809 A 20041123 ZA 2003-8809 20031112
PRIORITY APPLN. INFO.: US 2001-309065P P 20010731
WO 2002-IB2763 W 20020704

AB The present invention relates to pharmaceutical compns., kits and methods comprising combinations of lasofoxifene ((-)-cis-6-phenyl-5-[4- (2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol) or nontoxic pharmacol. acceptable acid addition salts thereof and estrogens. The present invention also relates to pharmaceutical compns., kits and methods comprising combinations of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1- yl-ethoxy)-phenyl]-5,6,7 ,8-tetrahydro-naphthalene-2-ol or nontoxic pharmacol. acceptable acid addition salts thereof, estrogens and progestins. In the examples provided, lasofoxifene tartrate alone or in combination with 17β-ethynylestradiol completely reversed ovariectomy-induced bone loss in rats and antagonized the uterine hypertrophy effects induced by the estrogen.

IT 180916-16-9, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene, estrogen and progestin for treatment of osteoporosis and sexual dysfunctions)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:82249 HCAPLUS Full-text
DOCUMENT NUMBER: 138:281406
TITLE: Localization of orexin-1 receptors to vagal afferent neurons in the rat and humans
AUTHOR(S): Burdyga, Galina; Lal, Simon; Spiller, David; Jiang, Wen; Thompson, David; Attwood, Stephen; Saeed, Shakeel; Grundy, David; Varro, Andrea; Dimaline, Rod; Dockray, Graham J.
CORPORATE SOURCE: Department of Physiology, University of Liverpool, Liverpool, UK
SOURCE: Gastroenterology (2003), 124(1), 129-139
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Orexin-A and -B are brain-gut peptides that stimulate food intake via orexin-R1 and -R2 receptors. Cholecystokinin (CCK) inhibits food intake via CCKA receptors expressed on vagal afferent neurons. The purpose of the study was to determine whether vagal afferent neurons express OX-R1 and OX-R2 and whether orexin-A inhibits responses to CCK. OX-R1 and -R2 expression by rat and human nodose ganglia was examined by reverse-transcriptase polymerase chain reaction (RT-PCR). Receptor localization was determined by immunohistochem. Responses of rat jejunal afferent fibers were examined by electrophysiol. Both rat and human nodose ganglia expressed OX-R1 as detected by RT-PCR, and humans also expressed OX-R2. The identity of the products was confirmed by sequencing. Immunohistochem. indicated expression of OX-R1 in both species in neurons that also expressed CCKA and leptin receptors. In human ganglia there was also expression in glial cells that was absent in rats. Orexin-A had no effect on the resting discharge of afferent nerve fibers but inhibited responses to CCK. OX-R1 and CCKA receptors are expressed by human and rat vagal afferent neurons. Orexin inhibits responses to CCK suggesting a role in modulation of gut to brain signaling.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

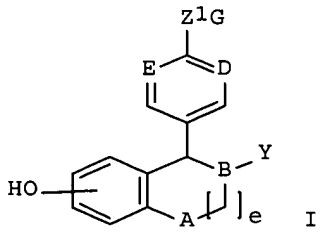
L18 ANSWER 14 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:52767 HCAPLUS Full-text
DOCUMENT NUMBER: 139:358454
TITLE: Pyrazolinone-piperidine dipeptide growth hormone secretagogues (GHSs): discovery of capromorelin
AUTHOR(S): Carpino, Philip A.; Lefker, Bruce A.; Toler, Steven M.; Pan, Lydia C.; Hadcock, John R.; Cook, Ewell R.; DiBrino, Joseph N.; Campeta, Anthony M.; DeNinno, Shari L.; Chidsey-Frink, Kristin L.; Hada, William A.; Inthavongsay, John; Mangano, F. Michael; Mullins, Michelle A.; Nickerson, David F.; Ng, Oicheng; Pirie, Christine M.; Ragan, John A.; Rose, Colin R.; Tess, David A.; Wright, Ann S.; Yu, Li; Zawistoski, Michael P.; DaSilva-Jardine, Paul A.; Wilson, Theresa C.; Thompson, David D.
CORPORATE SOURCE: Groton Labs, Pfizer Global Research and Development, Groton, CT, 06340, USA
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(4), 581-590
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:358454
AB Novel pyrazolinone-piperidine dipeptide derivs. were synthesized and evaluated as growth hormone secretagogues (GHSs). Two analogs, capromorelin (5, CP-424391-18, hGHS-R1a Ki=7 nM, rat pituicyte EC50=3 nM) and the des-Me analog 5c (hGHS-R1a Ki=17 nM, rat pituicyte EC50=3 nM), increased plasma GH levels in an anesthetized rat model, with ED50 values less than 0.05 mg/kg iv. Capromorelin showed enhanced intestinal absorption in rodent models and exhibited superior pharmacokinetic properties, including high bioavailabilities in two animal species [F(rat)=65%, F(dog)=44%]. This short-duration GHS was orally active in canine models and was selected as a development candidate for the treatment of musculoskeletal frailty in elderly adults.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:847483 HCAPLUS Full-text
DOCUMENT NUMBER: 137:333165
TITLE: Methods and kits using an estrogen agonist/antagonist for treating depression or preventing deterioration of cognitive function
INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Petrie, Charles David; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 1254662 | A2 | 20021106 | EP 2002-252391 | | 20020402 |
| EP 1254662 | A3 | 20030521 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| AU 2002027566 | A5 | 20021031 | AU 2002-27566 | | 20020321 |
| CN 1382440 | A | 20021204 | CN 2002-105674 | | 20020417 |
| CA 2383175 | A1 | 20021025 | CA 2002-2383175 | | 20020423 |
| US 2003092719 | A1 | 20030515 | US 2002-132907 | | 20020424 |
| HU 200201356 | A2 | 20030828 | HU 2002-1356 | | 20020424 |
| NZ 518569 | A | 20030926 | NZ 2002-518569 | | 20020424 |
| ZA 2002003253 | A | 20031024 | ZA 2002-3253 | | 20020424 |
| JP 2002332232 | A | 20021122 | JP 2002-123544 | | 20020425 |
| US 2005080099 | A1 | 20050414 | US 2004-956896 | | 20040930 |
| PRIORITY APPLN. INFO.: | | | US 2001-286433P | P | 20010425 |
| | | | US 2002-132907 | A3 | 20020424 |

OTHER SOURCE(S): MARPAT 137:333165
GI




I

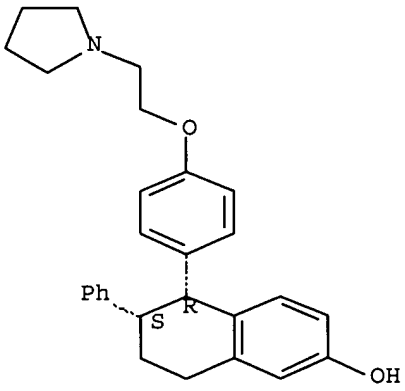
AB The invention provides methods and kits for treating depression, perimenopausal depression, schizophrenia, anxiety, panic attacks, binge eating, social phobia, or preventing deterioration of cognitive function by administering to a patient in need thereof a therapeutically effect amount of an estrogen agonist/antagonist I [A = CH2, NR; R = H, C1-6 alkyl; B, D, E = CH, N; Y = (substituted) Ph, (substituted) naphthyl, (substituted) C3-8 cycloalkyl, etc.; Z1 = OCHR2CHR3, SCHR2CHR3, etc.; R2, R3 = H, C1-4 alkyl; G =

NR7R8, C5-12 bicyclic amine, etc.; R7, R8 = Ph, C3-10 (un)saturated carbocyclic ring, etc.; e = 0-2].

IT 180916-16-9 180916-16-9D, isomers and derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonist/antagonist for treating depression and other conditions)

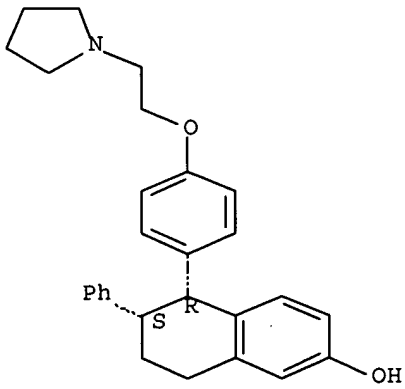
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:314396 HCAPLUS Full-text
DOCUMENT NUMBER: 136:319399
TITLE: Use of an estrogen agonist/antagonist for improving vascular health

INVENTOR(S): Day, Wesley W.; Lee, Andrew G.; Thompson, D.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

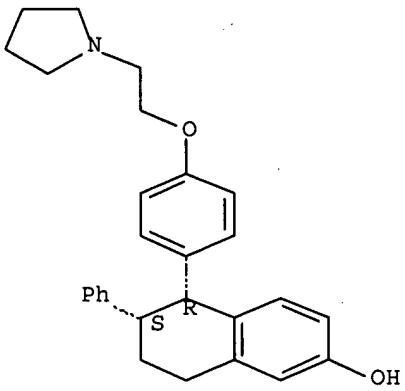
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1199071 | A2 | 20020424 | EP 2001-308806 | 20011016 |
| EP 1199071 | A3 | 20031029 | | |
| EP 1199071 | B1 | 20060524 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| AU 778095 | B2 | 20041118 | AU 2001-79392 | 20011012 |
| CA 2358840 | A1 | 20020417 | CA 2001-2358840 | 20011015 |
| US 2002156090 | A1 | 20021024 | US 2001-977458 | 20011015 |
| US 6620806 | B2 | 20030916 | | |
| ZA 2001008444 | A | 20030415 | ZA 2001-8444 | 20011015 |
| JP 2002145773 | A | 20020522 | JP 2001-317833 | 20011016 |
| HU 200104338 | A2 | 20020729 | HU 2001-4338 | 20011016 |
| NZ 514847 | A | 20030630 | NZ 2001-514847 | 20011016 |
| AT 326962 | T | 20060615 | AT 2001-308806 | 20011016 |
| PT 1199071 | T | 20060929 | PT 2001-308806 | 20011016 |

PRIORITY APPLN. INFO.: US 2000-241532P P 20001017
OTHER SOURCE(S): MARPAT 136:319399

AB The invention provides methods and kits for improving or maintaining vascular health, including preventing myocardial infarction or stroke; maintaining or improving vascular reactivity; treating acute or chronic renal failure, peripheral arterial occlusive disease, coronary artery disease, or Raynaud's phenomenon; or lowering plasma levels of Lp(a) using an estrogen agonist/antagonist.

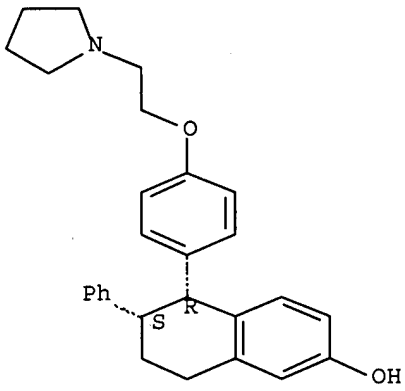
IT 180916-16-9 180916-16-9D, salts, N-oxides, and esters
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of estrogen agonist/antagonist for improving vascular health)
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



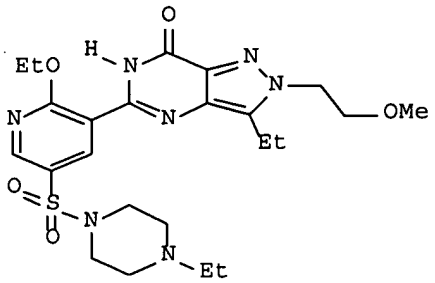
L18 ANSWER 17 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:640004 HCAPLUS Full-text
TITLE: Short- and long-acting growth hormone secretagogues (GHSs): Discovery and SAR of CP-424391-18 (capromorelin tartrate) and CP-464709-18
AUTHOR(S): Carpino, Philip A.; Lefker, Bruce A.; Toler, Steven M.; Pan, Lydia C.; Hadcock, John R.; Murray, Marianne C.; Cook, Ewell R.; Dibrino, Joseph N.; De Ninno, Shari L.; Chidsey-Frink, Kristin L.; Hada, William A.; Inthavongsay, John; Lewis, Sharon K.; Mangano, F. Michael; Mullins, Michelle A.; Nickerson, David F.; Ng, Oicheng; Pirie, Christine M.; Ragan, John A.; Rose, Colin R.; Tess, David A.; Wright, Ann S.; Yu, Li; Zawistoski, Michael P.; MacLean, David B. ; Pettersen, John C.; Da Silva-Jardine, Paul A.; Wilson, Theresa C.; Thompson, David D.
CORPORATE SOURCE: Department of Cardiovascular & Metabolic Diseases, Pfizer Global Research & Development - Groton Labs,

Groton, CT, 06340, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-185. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Growth hormone secretagogues (GHSs) are a new class of drugs that stimulate pituitary growth hormone (GH) secretion and increase plasma insulin growth factor-1 (IGF-1) levels. We have discovered a new series of pyrazolinone-piperidine dipeptide GHSs with good in vitro and in vivo activities. CP-424391-18 (capromorelin tartrate) is a short-acting GHS with good bioavailability in the beagle dog [dog t1/2=1.3 h; F(dog)=44%)]. CP-464709-18 is a longer-duration GHS that was identified from capromorelin by blocking potential sites of metabolism [dog t1/2=4.1 h; F(dog)=77%]. Both capromorelin and CP-464709-18 are in human clin. trials. The syntheses, pharmacol. characterizations and structure-activity relationships (SAR) of these GHSs will be presented.

L18 ANSWER 18 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:615491 HCAPLUS Full-text
DOCUMENT NUMBER: 135:180782
TITLE: Use of estrogen agonists/antagonists for the treatment of sexual dysfunction
INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 1125582 | A2 | 20010822 | EP 2001-300061 | | 20010105 |
| EP 1125582 | A3 | 20020417 | | | |
| EP 1125582 | B1 | 20060802 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR | | | | | |
| AT 334674 | T | 20060815 | AT 2001-300061 | | 20010105 |
| ZA 2001000176 | A | 20020708 | ZA 2001-176 | | 20010108 |
| CA 2331009 | A1 | 20010712 | CA 2001-2331009 | | 20010110 |
| CA 2331009 | C | 20051025 | | | |
| JP 2001233791 | A | 20010828 | JP 2001-2462 | | 20010110 |
| US 2001044434 | A1 | 20011122 | US 2001-757423 | | 20010110 |
| US 6512002 | B2 | 20030128 | | | |
| AU 784439 | B2 | 20060406 | AU 2001-11129 | | 20010110 |
| NZ 509320 | A | 20020628 | NZ 2001-509320 | | 20010111 |
| HU 200100121 | A2 | 20021028 | HU 2001-121 | | 20010111 |
| US 2003114440 | A1 | 20030619 | US 2002-301930 | | 20021121 |
| PRIORITY APPLN. INFO.: | | | US 2000-175704P | P | 20000112 |
| | | | US 2001-757423 | A3 | 20010110 |

OTHER SOURCE(S): MARPAT 135:180782
GI



I

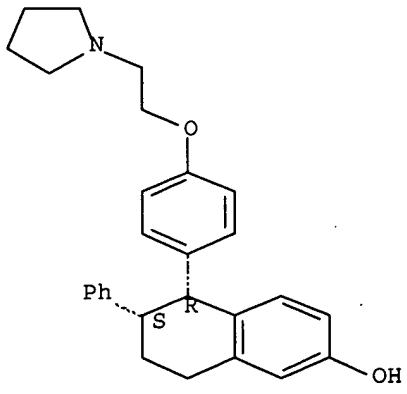
AB Pyridinylpyrazolopyrimidinone cGMP PDEv inhibitors, e.g., I were prepared Data for biol. activity of 3-[1-[4-(2-dimethylaminoethoxy)phenyl]-2-phenyl- 1-butenyl]phenol were given.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of estrogen agonists/antagonists for the treatment of sexual dysfunction)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 19 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:555210 HCAPLUS Full-text

DOCUMENT NUMBER: 135:142233

TITLE: Pharmaceutical compositions containing estrogen agonist/antagonist and statins for treatment of osteoporosis and/or for lowering blood cholesterol

INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| JP 2001206845 | A | 20010731 | JP 2001-15626 | | 20010124 |
| EP 1123717 | A2 | 20010816 | EP 2001-300527 | | 20010122 |
| EP 1123717 | A3 | 20031015 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| US 2003162807 | A1 | 20030828 | US 2001-767625 | | 20010123 |
| US 6756401 | B2 | 20040629 | | | |
| CA 2332214 | A1 | 20010726 | CA 2001-2332214 | | 20010124 |
| ZA 2001000675 | A | 20020724 | ZA 2001-675 | | 20010124 |
| AU 2001016675 | A5 | 20010802 | AU 2001-16675 | | 20010125 |
| AU 780568 | B2 | 20050407 | | | |
| HU 200100388 | A2 | 20030828 | HU 2001-388 | | 20010125 |
| NZ 523651 | A | 20040625 | NZ 2001-523651 | | 20010125 |
| US 2004259886 | A1 | 20041223 | US 2004-840577 | | 20040506 |
| AU 2005200655 | A1 | 20050310 | AU 2005-200655 | | 20050214 |
| PRIORITY APPLN. INFO.: | | | US 2000-188923P | P | 20000126 |
| | | | US 2000-205327P | P | 20000421 |
| | | | US 2001-767625 | A3 | 20010123 |

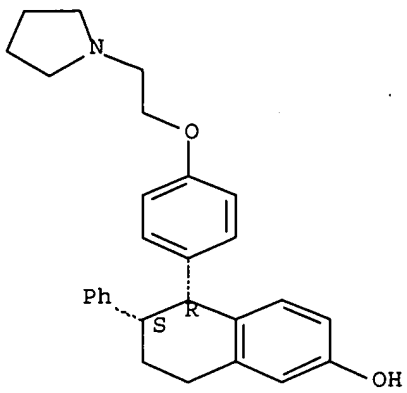
OTHER SOURCE(S): MARPAT 135:142233

AB The invention provides a composition containing an estrogen agonist/antagonist, and a statin deriv for treatment of osteoporosis and/or for lowering blood cholesterol. The antiosteoporotic effect of (-)-cis-6-phenyl-5-[4-(2- pyrrolidine-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol (PPTN) in ovary-excised rats were examined

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing estrogen agonist/antagonist and statins for treatment of osteoporosis and/or for lowering blood cholesterol)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 20 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:541600 HCAPLUS Full-text
DOCUMENT NUMBER: 135:117261
TITLE: Method using estrogen agonists/antagonists for reducing morbidity and the risk of mortality from cardiovascular disease, breast cancer, and osteoporosis
INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

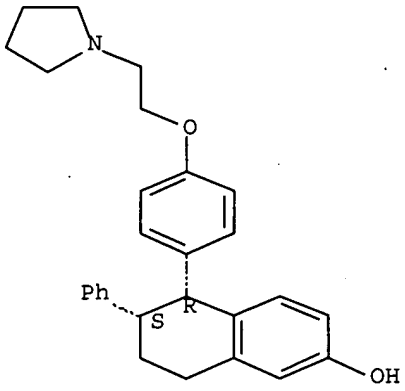
| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 1118323 | A2 | 20010725 | EP 2001-300159 | | 20010109 |
| EP 1118323 | A3 | 20030521 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| CA 2331059 | A1 | 20010712 | CA 2001-2331059 | | 20010110 |
| US 2001056099 | A1 | 20011227 | US 2001-757817 | | 20010110 |
| ZA 2001000276 | A | 20020710 | ZA 2001-276 | | 20010110 |
| HU 200100119 | A2 | 20021028 | HU 2001-119 | | 20010111 |
| JP 2001226265 | A | 20010821 | JP 2001-5300 | | 20010112 |
| PRIORITY APPLN. INFO.: | | | US 2000-175663P | P | 20000112 |

OTHER SOURCE(S): MARPAT 135:117261

AB The invention discloses methods, pharmaceutical compns., and kits useful in reducing cardiovascular morbidity and the risk of mortality in men and post-menopausal women and morbidity and the risk of mortality in post-menopausal women from the combined reduction of breast cancer, osteoporosis and cardiovascular disease by the administration of estrogen agonists/antagonists. The compns. are comprised of an estrogen agonist/antagonist and a pharmaceutically acceptable vehicle, carrier, or diluent. The compns. and methods of treatment are effective while substantially reducing the concomitant liability of adverse effects associated with estrogen administration.

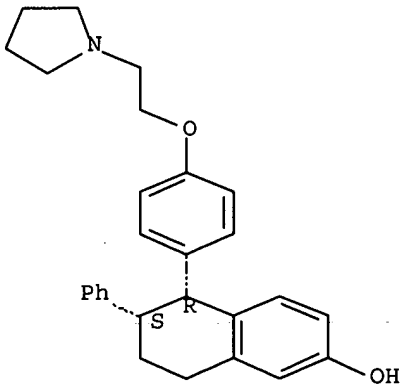
IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(estrogen agonists/antagonists for reducing morbidity and risk of mortality from cardiovascular disease, breast cancer, and osteoporosis)
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




IT 180916-16-9D, isomers, N-oxides, esters, and prodrug derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists/antagonists for reducing morbidity and risk of mortality from cardiovascular disease, breast cancer, and osteoporosis)
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 21 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:454559 HCAPLUS Full-text
DOCUMENT NUMBER: 138:100848
TITLE: Preclinical pharmacology of CP-424,391, an orally active pyrazolidinone-piperidine growth hormone secretagogue. [Erratum to document cited in CA135:87127]
AUTHOR(S): Pan, Lydia C.; Carpino, Philip A.; Lefker, Bruce A.; Ragan, John A.; Toler, Steven M.; Pettersen, John C.; Nettleton, David O.; Ng, Oicheng; Pirie, Christine M.; Chidsey-Frink, Kristin; Lu, Bihong; Nickerson, David F.; Tess, David A.; Mullins, Michelle A.; MacLean, David B.; Da Silva-Jardine, Paul A.; Thompson, David D.
CORPORATE SOURCE: Global Research & Development, Pfizer Inc., Groton, CT, USA
SOURCE: Endocrine (2001), 14(3), 437
CODEN: EOCRE5; ISSN: 1355-008X
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the article, CP-424,391 was incorrectly described as a pyrazolidinone-piperidine dipeptide; it should be a pyrazolinone- piperidine dipeptide GHS.

L18 ANSWER 22 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:274749 HCAPLUS Full-text
DOCUMENT NUMBER: 135:205314
TITLE: Lasofoxifene (CP-336,156) protects against the age-related changes in bone mass, bone strength, and total serum cholesterol in intact aged male rats
AUTHOR(S): Ke, Hua Zhu; Qi, Hong; Chidsey-Frink, Kristin L.; Crawford, D. Todd; Thompson, David D.
CORPORATE SOURCE: Osteoporosis Research, Department of Cardiovascular and Metabolic Diseases, Global Research and Development, Pfizer, Incorporated, Groton, CT, USA
SOURCE: Journal of Bone and Mineral Research (2001), 16(4), 765-773
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to evaluate if long-term (6 mo) treatment with lasofoxifene (LAS), a new selective estrogen receptor modulator (SERM), can protect against age-related changes in bone mass and bone strength in intact aged male rats. Sprague-Dawley male rats at 15 mo of age were treated (daily oral gavage) with either vehicle (n = 12) or LAS at 0.01 mg/kg per day (n = 12) or 0.1 mg/kg per day (n = 11) for 6 mo. A group of 15 rats was necropsied at 15 mo of age and served as basal controls. No significant change was found in body weight between basal and vehicle controls. However, an age-related increase in fat body mass (+42%) and decrease in lean body mass (-8.5%) was observed in controls. Compared with vehicle controls, LAS at both doses significantly decreased body weight and fat body mass but did not affect lean body mass. No significant difference was found in prostate wet weight among all groups. Total serum cholesterol was significantly decreased in all LAS-treated rats compared with both the basal and the vehicle controls. Both doses of LAS treatment completely prevented the age-related increase in serum osteocalcin. Peripheral quant. computerized tomog. (pQCT) anal. at the distal

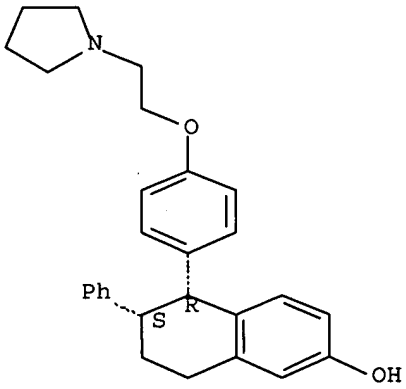
femoral metaphysis indicated that the age-related decrease in total d., trabecular d., and cortical thickness was completely prevented by treatment with LAS at 0.01 mg/kg per day or 0.1 mg/kg per day. Histomorphometric anal. of proximal tibial cancellous bone showed an age-related decrease in trabecular bone volume (TBV; -46%), trabecular number (Tb.N), wall thickness (W.Th), mineral apposition rate, and bone formation rate-tissue area referent. Moreover, an age-related increase in trabecular separation (Tb.Sp) and eroded surface was observed LAS at 0.01 mg/kg per day or 0.1 mg/kg per day completely prevented these age-related changes in bone mass, bone structure, and bone turnover. Similarly, the age-related decrease in TBV and trabecular thickness (Tb.Th) and the age-related increase in osteoclast number (Oc.N) and osteoclast surface (Oc.S) in the third lumbar vertebral cancellous bone were completely prevented by treatment with LAS at both doses. Further, LAS at both doses completely prevented the age-related decrease in ultimate strength (-47%) and stiffness (-37%) of the fifth lumbar vertebral body. These results show that treatment with LAS for 6 mo in male rats completely prevents the age-related decreases in bone mass and bone strength by inhibiting the increased bone resorption and bone turnover associated with aging. Further, LAS reduced total serum cholesterol and did not affect the prostate weight in these rats. Our data support the potential use of a SERM for protecting against the age-related changes in bone and serum cholesterol in elderly men.

IT 180916-16-9, Lasofoxifene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene (CP-336,156) protects against age-related changes in bone mass, bone strength, and total serum cholesterol in intact aged male rats)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:254834 HCAPLUS Full-text
DOCUMENT NUMBER: 134:261225
TITLE: Dosage plan of lasofoxifene and related

estrogen agonists and antagonists
INVENTOR(S): Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2001097862 | A | 20010410 | JP 2000-297908 | 20000929 |
| US 6436977 | B1 | 20020820 | US 2000-656273 | 20000906 |
| AU 781828 | B2 | 20050616 | AU 2000-56618 | 20000911 |
| EP 1092431 | A2 | 20010418 | EP 2000-308152 | 20000919 |
| EP 1092431 | A3 | 20020213 | | |
| EP 1092431 | B1 | 20060913 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY | | | | |
| AT 339201 | T | 20061015 | AT 2000-308152 | 20000919 |
| TW 224001 | B | 20041121 | TW 2000-89119761 | 20000925 |
| ZA 2000005141 | A | 20020326 | ZA 2000-5141 | 20000926 |
| CA 2321369 | A1 | 20010329 | CA 2000-2321369 | 20000927 |
| HU 200003836 | A2 | 20011028 | HU 2000-3836 | 20000928 |
| NZ 507200 | A | 20041224 | NZ 2000-507200 | 20000928 |
| NZ 516413 | A | 20041224 | NZ 2000-516413 | 20000928 |

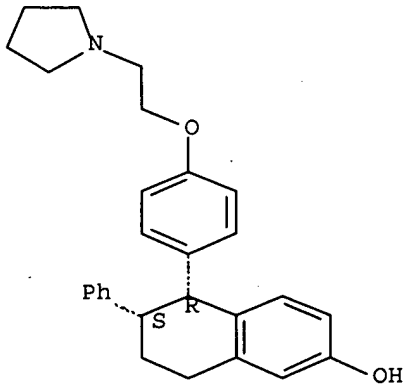
PRIORITY APPLN. INFO.: US 1999-156652P P 19990929

AB Lasofoxifene and related estrogen agonists and antagonists are given orally at 0.8-20 mg for 1-4 wks. for maintaining sustained blood levels for therapeutical purpose.

IT 180916-16-9, Lasofoxifene
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dosage plan of lasofoxifene and related estrogen agonists and antagonists)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 24 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:257767 HCAPLUS Full-text
DOCUMENT NUMBER: 133:26826
TITLE: Lasofoxifene (CP-336,156), a selective estrogen receptor modulator, prevents bone loss induced by aging and orchidectomy in the adult rat
AUTHOR(S): Ke, Hua Zhu; Qi, Hong; Crawford, D. Todd; Chidsey-Frink, Kristin L.; Simmons, Hollis A.; Thompson, David D.
CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases, Central Research Division, Pfizer, Inc., Groton, CT, 06340, USA
SOURCE: Endocrinology (2000), 141(4), 1338-1344
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been well documented that selective estrogen receptor modulators (SERMs) can prevent bone loss in ovariectomized rats and postmenopausal women. The purposes of this study were to determine the effects of a potent and orally active SERM, lasofoxifene (CP-336,156), on bone mass, bone strength, total serum cholesterol, prostate weight, and histol. in adult male orchidectomized (ORX) rats. Sprague Dawley male rats at 10 mo of age were divided into 6 groups, with 10 rats/group. The first group was necropsied on day 0 and served as basal controls. The remaining rats were either sham operated (n = 10) and treated orally with vehicle, or ORX (n = 40) and treated with either vehicle or lasofoxifene at 1, 10, or 100 μg/kg·day for 60 days. Total serum cholesterol, prostate weight and histol., distal femoral bone mineral d. (DFBMD) by dual energy x-ray absorptiometry, and static and dynamic bone histomorphometry of the third lumbar vertebral body were determined Maximal load and stiffness of the fifth lumbar vertebral body were also determined by compression tests. Age-related decreases in DFBMD (-9%) and trabecular bone volume (TBV; -13%) of the third lumbar vertebral body were found in sham-operated rats compared with basal controls. ORX induced significant increases in total serum cholesterol (+31%), eroded surface (+48%), activation frequency of bone turnover (+103%) and significant decreases in prostate weight (-89%), DFBMD (-14%), TBV (-23%), and maximal load (-17%) compared with basal controls. Compared with sham controls, ORX induced significant increases in eroded perimeter and activation frequency. Lasofoxifene decreased body weight in all dose groups compared with both sham and ORX control values. Compared with ORX controls, ORX rats treated with lasofoxifene at 10 or 100 μg/kg·day had significantly lower percent eroded perimeter activation frequency and significantly higher DFBMD, TBV, and maximal load. Further, lasofoxifene at 10 and 100 μg/kg·day significantly decreased total serum cholesterol by 46% and 68% in ORX rats, whereas no effect was found in prostate weight and histol. parameters compared with ORX control values. These data showed that lasofoxifene prevented bone loss by inhibiting bone turnover associated with aging and orchidectomy in 10-mo-old male rats. Further, lasofoxifene decreased total serum cholesterol and did not affect the prostate in these rats. These results suggest that SERMs such as lasofoxifene may be useful therapeutic agents for preventing bone loss in elderly men with some degree of hypogonadism.

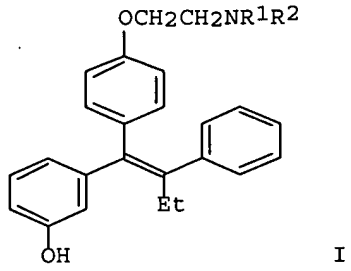
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:68983 HCAPLUS Full-text
DOCUMENT NUMBER: 132:102844
TITLE: Method of increasing testosterone with droloxifene or a related compound
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 5 pp., Cont. of U.S. Ser. No. 803,711, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 6017964 | A | 20000125 | US 1998-208729 | | 19981209 |
| PRIORITY APPLN. INFO.: | | | US 1996-21181P | P | 19960228 |
| | | | US 1997-803711 | B1 | 19970221 |

GI




I

AB Methods are provided for increasing serum levels of testosterone which comprise administering to a mammal in need of such treatment an effective amount of I (R1 and R2 may be the same or different, provided that when R1 and R2 are the same, each is Me or Et, and when R1 and R2 are different, one is Me or Et and the other is H or benzyl) or a pharmaceutically acceptable salt thereof.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 26 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:818996 HCAPLUS Full-text
DOCUMENT NUMBER: 132:44985
TITLE: Therapeutic combinations comprising a selective estrogen receptor modulator and prostaglandin E2
INVENTOR(S): Ke, Hua Zhu; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

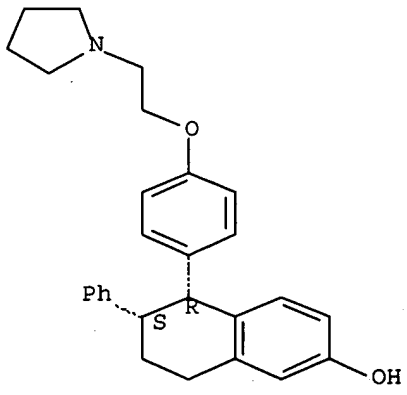
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 966968 | A1 | 19991229 | EP 1999-304374 | 19990604 |
| EP 966968 | B1 | 20040506 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| AT 265853 | T | 20040515 | AT 1999-304374 | 19990604 |
| PT 966968 | T | 20040831 | PT 1999-304374 | 19990604 |
| ES 2220005 | T3 | 20041201 | ES 1999-304374 | 19990604 |
| CA 2274381 | A1 | 19991216 | CA 1999-2274381 | 19990614 |
| CA 2274381 | C | 20040210 | | |
| JP 2000026298 | A | 20000125 | JP 1999-167503 | 19990614 |
| MX 9905564 | A | 20001130 | MX 1999-5564 | 19990615 |
| BR 9904146 | A | 20000509 | BR 1999-4146 | 19990616 |
| US 6284773 | B1 | 20010904 | US 1999-314371 | 19990714 |
| PRIORITY APPLN. INFO.: | | | US 1998-89468P P | 19980616 |

AB Combination compns. comprising (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol (I) or pharmaceutically acceptable salts and PGE2 or a pharmaceutically acceptable salt are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass and frailty. Expts. on rats show that I inhibits bone resorption and bone turnover, prevents further bone loss and preserves bone strength. Further I potentiates the bone restoration effects of PGE2 in established osteopenic rats.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic combinations comprising a selective estrogen receptor modulator and prostaglandin E2)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 27 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:811078 HCAPLUS Full-text
DOCUMENT NUMBER: 132:45000
TITLE: Therapeutic combinations of (selective) estrogen receptor modulators (SERM) and growth hormone secretagogues (GHS) for treating musculoskeletal frailty
INVENTOR(S): Ke, Hua Zhu; Li, Mei; Pan, Lydia Codetta; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9965488 | A1 | 19991223 | WO 1999-IB796 | | 19990503 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2335112 | A1 | 19991223 | CA 1999-2335112 | | 19990503 |
| AU 9933420 | A | 20000105 | AU 1999-33420 | | 19990503 |
| BR 9911357 | A | 20010313 | BR 1999-11357 | | 19990503 |
| EP 1085867 | A1 | 20010328 | EP 1999-914723 | | 19990503 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | | |
| HU 200102395 | A2 | 20011128 | HU 2001-2395 | | 19990503 |
| JP 2002518328 | T | 20020625 | JP 2000-554368 | | 19990503 |
| IN 1999DE00845 | A | 20050701 | IN 1999-DE845 | | 19990610 |
| ZA 9903973 | A | 20001215 | ZA 1999-3973 | | 19990615 |
| NO 2000006381 | A | 20001214 | NO 2000-6381 | | 20001214 |
| HR 2000000857 | A1 | 20011031 | HR 2000-857 | | 20001214 |
| BG 105128 | A | 20011130 | BG 2001-105128 | | 20010108 |
| PRIORITY APPLN. INFO.: | | | US 1998-89424P | P | 19980616 |
| | | | WO 1999-IB796 | W | 19990503 |

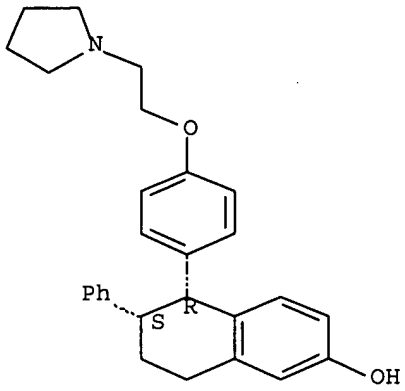
AB This invention is directed to pharmaceutical combination compns. and methods comprising (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)phenyl)- 5,6,7,8-tetrahydronaphthalene-2-ol or a pharmaceutically acceptable salt thereof and 2-amino-N-(1(R)-(2,4-difluorobenzyloxymethyl)-2-oxo-2-(3-oxo- 3a(R)pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7- hexahydropyrazolo[4,3-c]pyridin-5-yl)ethyl-2-methylpropionamide or a pharmaceutically acceptable salt thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass, frailty and low muscle mass.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 28 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:811077 HCAPLUS Full-text
DOCUMENT NUMBER: 132:44999
TITLE: Therapeutic combinations of (selective) estrogen receptor modulators (SERM) and growth hormone secretagogues (GHS) for treating musculoskeletal frailty
INVENTOR(S): Ke, Hua Zhu; Li, Mei; Pan, Lydia Codetta; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9965486 | A1 | 19991223 | WO 1999-IB1117 | 19990616 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9903975 | A | 20001215 | ZA 1999-3975 | 19990615 |
| CA 2335134 | A1 | 19991223 | CA 1999-2335134 | 19990616 |

| | | | | |
|---|---|---|---|---|
| AU 9940547 | A1 | 20000105 | AU 1999-40547 | 19990616 |
| BR 9911324 | A | 20010403 | BR 1999-11324 | 19990616 |
| EP 1087764 | A1 | 20010404 | EP 1999-923802 | 19990616 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200003544 | T2 | 20010420 | TR 2000-200003544 | 19990616 |
| HU 200102505 | A2 | 20011128 | HU 2001-2505 | 19990616 |
| JP 2002518326 | T | 20020625 | JP 2000-554366 | 19990616 |
| BG 105041 | A | 20010831 | BG 2000-105041 | 20001211 |
| NO 2000006312 | A | 20001212 | NO 2000-6312 | 20001212 |
| HR 2000000859 | A1 | 20010430 | HR 2000-859 | 20001214 |
| PRIORITY APPLN. INFO.: | | | US 1998-89469P P | 19980616 |
| | | | WO 1999-IB1117 W | 19990616 |

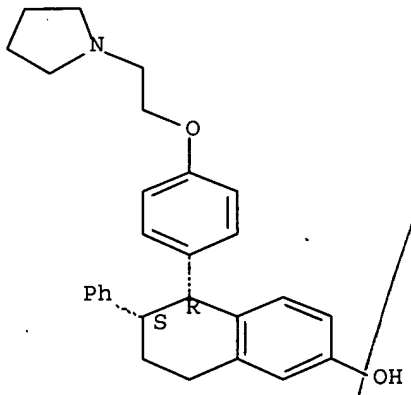
AB This invention is directed to pharmaceutical combination compns. and methods containing (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)phenyl)- 5,6,7,8-tetrahydronaphtalene-2-ol or a pharmaceutically acceptable salt thereof and 2-amino-N-(2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7- hexahydropyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo- ethyl)isobutyramide or a pharmaceutically acceptable salt thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass, frailty and low muscle mass.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:811074 HCAPLUS Full-text
DOCUMENT NUMBER: 132:30842
TITLE: Therapeutic combinations comprising a selective

estrogen receptor modulator and parathyroid hormone

INVENTOR(S): Ke, Hua Zhu; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

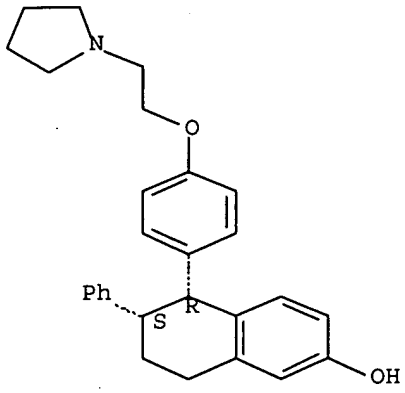
| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9965482 | A1 | 19991223 | WO 1999-IB949 | | 19990526 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2335078 | A1 | 19991223 | CA 1999-2335078 | | 19990526 |
| AU 9937259 | A1 | 20000105 | AU 1999-37259 | | 19990526 |
| BR 9911228 | A | 20010213 | BR 1999-11228 | | 19990526 |
| EP 1094808 | A1 | 20010502 | EP 1999-919491 | | 19990526 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | | |
| TR 200003567 | T2 | 20010621 | TR 2000-200003567 | | 19990526 |
| HU 200102759 | A2 | 20020328 | HU 2001-2759 | | 19990526 |
| JP 2002518323 | T | 20020625 | JP 2000-554362 | | 19990526 |
| NZ 508039 | A | 20030328 | NZ 1999-508039 | | 19990526 |
| ZA 9903972 | A | 20001215 | ZA 1999-3972 | | 19990615 |
| US 6132774 | A | 20001017 | US 1999-424010 | | 19991115 |
| NO 2000006313 | A | 20001212 | NO 2000-6313 | | 20001212 |
| HR 2000000858 | A1 | 20011031 | HR 2000-858 | | 20001214 |
| BG 105125 | A | 20011130 | BG 2001-105125 | | 20010108 |
| PRIORITY APPLN. INFO.: | | | US 1998-89479P | P | 19980616 |
| | | | WO 1999-IB949 | W | 19990526 |

AB This invention is directed to pharmaceutical combination compns. and methods comprising (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]- 5,6,7,8-tetrahydronaphthalen-2-ol (I) or a pharmaceutically acceptable salt thereof and parathyroid hormone (PTH) or a biol. active fragment thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass and frailty. Data showed that combined treatment of PTH and I both restored bone mass and bone strength to established osteopenic, rats, and added extra cancellous bone to the proximal tibia and distal femur of the rats. I enhanced the bone restorative effects of PTH by a greated inhibition of bone resorption than bone formation.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic combinations comprising selective estrogen receptor modulator and parathyroid hormone)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

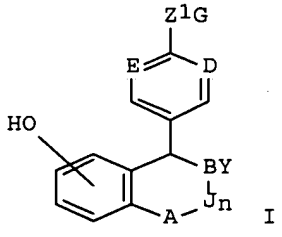



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 30 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:212801 HCAPLUS Full-text
DOCUMENT NUMBER: 130:262143
TITLE: Method of treating Alzheimer's disease and other diseases and conditions with estrogen agonists and antagonists
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5889042 | A | 19990330 | US 1997-803706 | 19970221 |

PRIORITY APPLN. INFO.: US 1997-803706 19970221
OTHER SOURCE(S): MARPAT 130:262143
GI



I

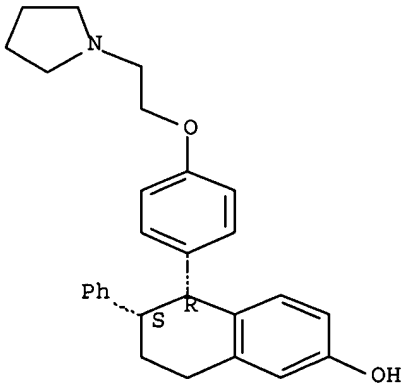
AB Compds. I [A = CH2, NR; B, D, E = CH, N; Y = (substituted) Ph, (substituted) naphthyl, (substituted) C3-8 cycloalkyl, etc.; J = CH2; Z1 = (CH2)pW(CH2)q, O(CH2)pW(CH2)q, etc.; G = NR7R8, heterocyclic ring; W = CH2, CH:CH, O, etc.; R = H, C1-6 alkyl; R7, R8 = H, Ph, C1-6 alkyl, etc.; n = 0-2; p, q = 0-3], and optical and geometric isomers and nontoxic pharmacol. acceptable acid addition salts, N-oxides, and quaternary ammonium salts thereof, are useful for treating or preventing Alzheimer's disease, premenstrual syndrome, peri-menopausal syndrome, a deficiency of thrombomodulin, uterine fibrosis, excessive myeloperoxidase activity, excessive thrombin, autoimmune disease, reperfusion damage of ischemic myocardium and insufficient testosterone. (-)-Cis-6-phenyl-5-[4-(2- pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol is claimed for inhibiting Alzheimer's disease.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists and antagonists for treatment of Alzheimer's disease and other diseases and conditions)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 31 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:56372 HCAPLUS Full-text
DOCUMENT NUMBER: 130:120020
TITLE: Combination therapy to prevent bone loss parathyroid hormone and estrogen agonists
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5861438 | A | 19990119 | US 1997-803712 | 19970221 |

PRIORITY APPLN. INFO.: US 1997-803712 19970221
OTHER SOURCE(S): MARPAT 130:120020
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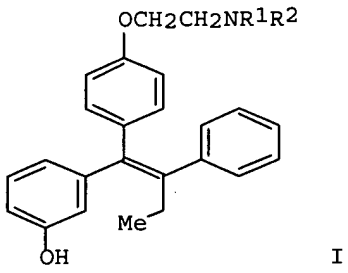



I

AB The present invention provides novel methods of inhibiting bone loss comprising administering to a mammal in need of such treatment an effective amount of a compound of formula (I) wherein R1 and R2 may be the same or different provided that, when R1 and R2 are the same, each is a Me or Et group, and, when R1 and R2 are different, one of them is a Me or Et group and the other is a hydrogen or a benzyl group; or a pharmaceutically acceptable salt thereof; together with or in combination with parathyroid hormone. Pharmaceutical compns. containing compds. of the invention are claimed as is a kit containing a therapeutic amount of a compound of formula I and a pharmaceutical carrier in a first unit dosage form plus a therapeutic amount of a parathyroid hormone and a pharmaceutical carrier in a second unit dosage form.

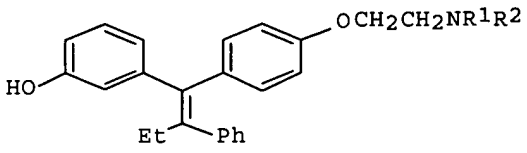
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 32 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:430074 HCAPLUS Full-text
DOCUMENT NUMBER: 129:100036
TITLE: Combination therapy to treat osteoporosis - polyphosphonates and estrogen agonists
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| US 5773477 | A | 19980630 | US 1997-803707 | 19970221 |
| PRIORITY APPLN. INFO.: | | | US 1997-803707 | 19970221 |
| OTHER SOURCE(S): | MARPAT 129:100036 | | | |

GI




I

AB A novel method of treating or preventing osteoporosis in mammals comprises administering an effective amount of an estrogen agonist (I; R1, R2 =, Me, Et, PhCH2; when R1 = R2, each is Me or Et; when R1 ≠ R2, one is Me or Et and the other is H or PhCH2) or pharmaceutically acceptable salt thereof, together with a bone resorption-inhibiting polyphosphonate. Thus, tablets were prepared containing active ingredients 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% aqueous solution) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 weight parts.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:202677 HCAPLUS Full-text
DOCUMENT NUMBER: 128:275095
TITLE: Pharmaceutical compositions containing dialkylaminoethoxyphenylhydroxyphenylphenyl butene for alleviating symptoms of premenstrual syndrome and late luteal phase dysphoric disorder
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5733937 | A | 19980331 | US 1997-804702 | 19970221 |
| PRIORITY APPLN. INFO.: | | | US 1997-804702 | 19970221 |
| OTHER SOURCE(S): | MARPAT 128:275095 | | | |

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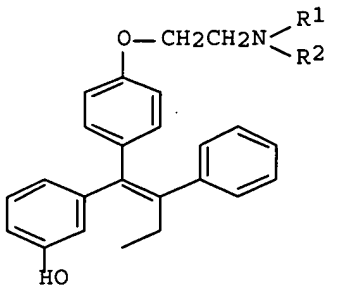



I

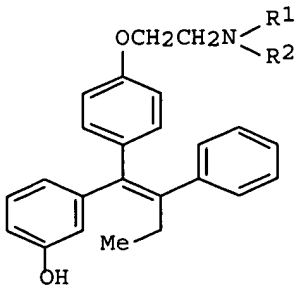
AB Novel methods of inhibiting the symptoms of premenstrual syndrome comprising administering to a human in need of treatment an effective amount of a compound of formula I (R1 and R2 may be the same or different provided that, when R1 and R2 are the same, each is a Me or Et group, and, when R1 and R2 are different, one of them is a Me or Et group and the other is hydrogen or a benzyl group), or a pharmaceutically acceptable salt thereof. A tablet contained active ingredient 0.25-100, starch 45, microcryst. cellulose 35, polyvinylpyrrolidone 4 (as 10% solution in water) sodium CM-cellulose 4.5, magnesium stearate 0.5, and talc 1 mg. Efficacy of 10-100 mg/day of the above drug by the oral route was studied for the inhibition of premenstrual syndrome and late luteal phase dysphoric disorder symptoms in women for a period of 1-3 mo.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 34 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:180551 HCAPLUS Full-text
DOCUMENT NUMBER: 128:248582
TITLE: Pharmaceutical composition for the protection of ischemic myocardium against reperfusion damage
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5726207 | A | 19980310 | US 1997-805040 | 19970221 |

PRIORITY APPLN. INFO.: US 1997-805040 19970221
OTHER SOURCE(S): MARPAT 128:248582
GI




I

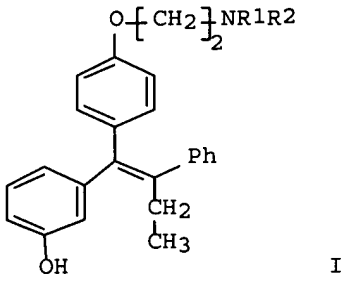
AB Novel methods of inhibiting reperfusion damage in ischemic myocardium comprise administering to a mammal in need of such treatment an effective amount of (I; R1 and R2 may be the same or different provided that, when R1 and R2 are the same, each is a Me or Et group, and, when R1 and R2 are different, one of them is a Me or Et group and the other is hydrogen or a benzyl group); or a pharmaceutically acceptable salt thereof. Hard gelatin capsules were prepared containing I 0.25-100, starch 0-650, starch flowable powder 0-50, silicone fluid 350 cSt 0-15 mg/capsule.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 35 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:146573 HCAPLUS Full-text
DOCUMENT NUMBER: 128:184707
TITLE: Pharmaceutical compositions containing 1,1,2-triphenylbut-1-ene derivatives for treating alzheimer's disease
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5719191 | A | 19980217 | US 1997-805039 | 19970221 |

PRIORITY APPLN. INFO.: US 1997-805039 19970221
OTHER SOURCE(S): MARPAT 128:184707
GI



I

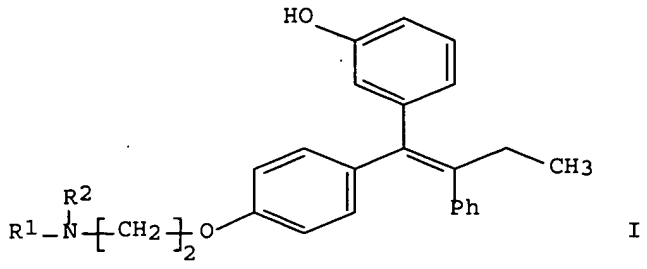
AB Novel methods of inhibiting Alzheimer's disease are provided comprising administering to a human in need of treatment an effective amount of a 1,1,2-triphenylbut-1-ene derivs. (I; R1 and R2 may be the same or different provided that, when R1 and R2 are the same, each is a Me or Et group, and, when R1 and R2 are different, one of them is a Me or Et group and the other is hydrogen or a benzyl group) or a pharmaceutically acceptable salt thereof. A hard gelatin capsule contained I 0.25, starch 650, starch flowable powder 50, and silicone fluid 350 cSt 15 mg. Efficacy of compound of formula I in decreasing lactate dehydrogenase (a neurotoxic) release from cultured primary rat hippocampal neurons was shown.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 36 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:146572 HCAPLUS Full-text
DOCUMENT NUMBER: 128:196689
TITLE: Pharmaceutical compositions containing myeloperoxidase inhibitors
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5719190 | A | 19980217 | US 1997-803709 | 19970221 |

PRIORITY APPLN. INFO.: US 1997-803709 19970221
OTHER SOURCE(S): MARPAT 128:196689
GI



I

AB Novel methods of inhibiting myeloperoxidase activity is provided comprising administering to a mammal in need of such treatment an effective amount of a compound I (R1, R2 may be the same or different provided that, when R1 and R2 are the same, each is a Me or Et, and when R1 and R2 are different, one of them is a Me or Et and the other is hydrogen or a benzyl) or a pharmaceutically acceptable salt thereof. A tablet contained active ingredient 100, starch 45, microcryst. cellulose 35, polyvinylpyrrolidone 4 (as 10% solution in water) sodium CM-cellulose 4.5, magnesium stearate 0.5, and talc 1 mg. Efficacy of I in treatment of women suffering from systemic lupus erythematosus and arthritis is shown.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 37 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:610807 HCAPLUS Full-text
DOCUMENT NUMBER: 127:253203
TITLE: Use of droloxifene for the manufacture of a medicament for increasing serum levels of testosterone
INVENTOR(S): MaClean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 793961 | A1 | 19970910 | EP 1997-301171 | 19970221 |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| IL 120262 | A | 20010128 | IL 1997-120262 | 19970220 |
| JP 09315962 | A | 19971209 | JP 1997-39077 | 19970224 |
| CA 2198535 | A1 | 19970828 | CA 1997-2198535 | 19970226 |
| CA 2198535 | C | 20000620 | | |
| AU 9714966 | A | 19970904 | AU 1997-14966 | 19970227 |
| AU 712800 | B2 | 19991118 | | |
| ZA 9701709 | A | 19980827 | ZA 1997-1709 | 19970227 |
| CN 1165649 | A | 19971126 | CN 1997-103408 | 19970228 |
| PRIORITY APPLN. INFO.: | | | US 1996-21181P P | 19960228 |

OTHER SOURCE(S): MARPAT 127:253203

AB 3-[1-[4-(2-Aminoethoxy)phenyl]-2-phenyl-1-butenyl]phenol derivs., preferably droloxifene, are used for the manufacture of a medicament for increasing serum levels of testosterone. Formulations for capsules, tablets, suspensions,

aerosols, suppositories, and i.v. solns. are provided. Administration of droloxifene to men (62-75 yr old) at 10 and 40 mg per day significantly increased testosterone levels.

L18 ANSWER 38 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:600540 HCAPLUS Full-text
DOCUMENT NUMBER: 127:243268
TITLE: Method of treating conditions with estrogen agonists
INVENTOR(S): Maclean, David Burton; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 792642 | A1 | 19970903 | EP 1997-301150 | 19970221 |
| EP 792642 | B1 | 20010822 | | |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| TW 442286 | B | 20010623 | TW 1997-86100636 | 19970121 |
| IL 120267 | A | 20021110 | IL 1997-120267 | 19970220 |
| AT 204475 | T | 20010915 | AT 1997-301150 | 19970221 |
| ES 2159812 | T3 | 20011016 | ES 1997-301150 | 19970221 |
| CA 2198562 | A1 | 19970828 | CA 1997-2198562 | 19970226 |
| CA 2198562 | C | 20020910 | | |
| AU 9714980 | A | 19970904 | AU 1997-14980 | 19970227 |
| AU 703384 | B2 | 19990325 | | |
| ZA 9701713 | A | 19980827 | ZA 1997-1713 | 19970227 |
| CN 1165655 | A | 19971126 | CN 1997-103415 | 19970228 |
| JP 10007564 | A | 19980113 | JP 1997-45905 | 19970228 |
| GR 3036874 | T3 | 20020131 | GR 2001-401737 | 20011011 |

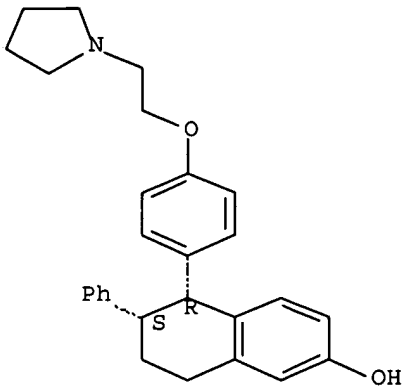
PRIORITY APPLN. INFO.: US 1996-13213P P 19960228 ✓
OTHER SOURCE(S): MARPAT 127:243268

AB Estrogen agonists such as cis-6-(40fluorophenyl)5-[4-(2-piperidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol are used to treat pathol. condition such as Alzheimer's disease, premenstrual syndrome, premenopausal syndrome, a deficiency of thrombomodulin, uterine fibrosis, excessive myeloperoxidase activity, excessive thrombin, autoimmune disease, reperfusion damage of ischemic myocardium and insufficient testosterone.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists for treatment of pathol. conditions)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 39 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:600513 HCAPLUS Full-text
DOCUMENT NUMBER: 127:253197
TITLE: Combination therapy to treat osteoporosis
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 792645 | A1 | 19970903 | EP 1997-301174 | | 19970221 |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | | |
| CA 2198534 | A1 | 19970828 | CA 1997-2198534 | | 19970226 |
| AU 9714976 | A | 19970904 | AU 1997-14976 | | 19970227 |
| CN 1165654 | A | 19971126 | CN 1997-103409 | | 19970228 |
| JP 10007562 | A | 19980113 | JP 1997-45060 | | 19970228 |
| CN 1178668 | A | 19980415 | CN 1997-103412 | | 19970228 |
| PRIORITY APPLN. INFO.: | | | US 1996-13367P | P | 19960228 |

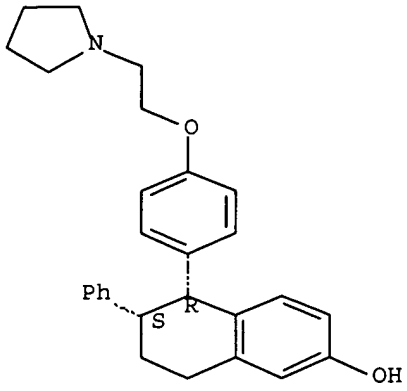
OTHER SOURCE(S): MARPAT 127:253197

AB A pharmaceutical composition comprising a compound such as cis-6-(4-fluorophenyl)- 5-[4-(2-piperidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol in combination with a bone resorption inhibiting polyphosphonate or a progestin is useful for treating or preventing osteoporosis.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonist in combination with polyphosphonate or progestin in treatment of osteoporosis)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 40 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:600476 HCAPLUS Full-text
DOCUMENT NUMBER: 127:253196
TITLE: Use of (E)-1-(4-(2-alkylaminoethoxy)phenyl)-1-(3-hydroxyphenyl)-2-phenylbut-1-enes for inhibiting pathological conditions
INVENTOR(S): Maclean, David Burton; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 792640 | A2 | 19970903 | EP 1997-301149 | 19970221 |
| EP 792640 | A3 | 19980708 | | |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| US 5985932 | A | 19991116 | US 1997-804346 | 19970221 |
| CA 2198571 | A1 | 19970828 | CA 1997-2198571 | 19970226 |
| AU 9714956 | A | 19970904 | AU 1997-14956 | 19970226 |
| AU 707455 | B2 | 19990708 | | |
| ZA 9701710 | A | 19980827 | ZA 1997-1710 | 19970227 |
| CN 1165651 | A | 19971126 | CN 1997-103416 | 19970228 |
| JP 09328421 | A | 19971222 | JP 1997-45616 | 19970228 |
| PRIORITY APPLN. INFO.: | | | US 1996-12401P | P 19960228 |
| | | | US 1996-12402P | P 19960228 |
| | | | US 1996-12403P | P 19960228 |
| | | | US 1996-12404P | P 19960228 |
| | | | US 1996-12410P | P 19960228 |
| | | | US 1996-12411P | P 19960228 |

OTHER SOURCE(S): MARPAT 127:253196
AB (E)-1-(4-(2-alkylaminoethoxy)phenyl)-1-(3-hydroxyphenyl)-2-phenylbut-1-enes are used for the manufacture of a medicament for inhibiting a condition selected from pathol. conditions related to organ systems which respond to

estrogen agonists, uterine fibrosis, myeloperoxidase activity, autoimmune diseases, reperfusion damage in ischemic myocardium, and the symptoms of premenstrual syndrome. An example compound is droloxifene and a number of pharmaceutical formulations were given.

L18 ANSWER 41 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:600459 HCAPLUS Full-text
DOCUMENT NUMBER: 127:239138
TITLE: Combination therapy to treat osteoporosis or conditions which present low bone mass
INVENTOR(S): Maclean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 792639 | A1 | 19970903 | EP 1997-301148 | | 19970221 |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | | |
| CA 2198580 | A1 | 19970828 | CA 1997-2198580 | | 19970226 |
| CA 2198580 | C | 20010703 | | | |
| AU 9714978 | A | 19970904 | AU 1997-14978 | | 19970227 |
| AU 718242 | B2 | 20000413 | | | |
| ZA 9701711 | A | 19980827 | ZA 1997-1711 | | 19970227 |
| CN 1166316 | A | 19971203 | CN 1997-103406 | | 19970228 |
| JP 09328430 | A | 19971222 | JP 1997-45288 | | 19970228 |
| US 6100301 | A | 20000808 | US 1998-92100 | | 19980605 |
| PRIORITY APPLN. INFO.: | | | US 1996-12399P | P | 19960228 |
| | | | US 1996-12409P | P | 19960228 |

OTHER SOURCE(S): MARPAT 127:239138
AB Aminoethoxyphenyl hydroxy Et stilbene derivs. together with a bone resorption inhibiting polyphosphonate or parathyroid hormone are useful for treating osteoporosis and that containing parathyroid hormone, for treating a condition which presents low bone mass. An example compound is droloxifene.

L18 ANSWER 42 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:600450 HCAPLUS Full-text
DOCUMENT NUMBER: 127:243267
TITLE: Use of estrogen antagonists and estrogen agonists in inhibiting pathological conditions
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| EP 792641 | A1 | 19970903 | EP 1997-301147 | 19970221 |
| EP 792641 | B1 | 20010801 | | |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| IL 120266 | A | 20050517 | IL 1997-120266 | 19970220 |
| US 6107331 | A | 20000822 | US 1997-803733 | 19970221 |
| EP 1106179 | A2 | 20010613 | EP 2001-101953 | 19970221 |
| EP 1106179 | A3 | 20040107 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| AT 203670 | T | 20010815 | AT 1997-301147 | 19970221 |
| ES 2159811 | T3 | 20011016 | ES 1997-301147 | 19970221 |
| CA 2198578 | A1 | 19970828 | CA 1997-2198578 | 19970226 |
| CA 2198578 | C | 20020611 | | |
| ZA 9701714 | A | 19970827 | ZA 1997-1714 | 19970227 |
| AU 9714979 | A | 19970904 | AU 1997-14979 | 19970227 |
| AU 703473 | B2 | 19990325 | | |
| CN 1167617 | A | 19971217 | CN 1997-103414 | 19970228 |
| CN 1122513 | B | 20031001 | | |
| JP 10007563 | A | 19980113 | JP 1997-45652 | 19970228 |
| CN 1515256 | A | 20040728 | CN 2003-2003141228 | 19970228 |
| HK 1001963 | A1 | 20040130 | HK 1998-101068 | 19980212 |
| US 6274618 | B1 | 20010814 | US 1999-314758 | 19990519 |
| US 6355670 | B1 | 20020312 | US 2000-511806 | 20000223 |
| US 2001018451 | A1 | 20010830 | US 2001-803516 | 20010309 |
| US 6403611 | B2 | 20020611 | | |
| GR 3036583 | T3 | 20011231 | GR 2001-401440 | 20010911 |
| US 2002091121 | A1 | 20020711 | US 2001-999291 | 20011115 |
| US 6613796 | B2 | 20030902 | | |
| US 2003220349 | A1 | 20031127 | US 2002-133006 | 20020426 |
| US 6911456 | B2 | 20050628 | | |
| US 2004009994 | A1 | 20040115 | US 2003-615282 | 20030707 |
| US 2005148625 | A1 | 20050707 | US 2005-71955 | 20050303 |
| PRIORITY APPLN. INFO.: | | | US 1996-13212P | P 19960228 |
| | | | EP 1997-301147 | A3 19970221 |
| | | | US 1997-803733 | A1 19970221 |
| | | | US 1999-314758 | A1 19990519 |
| | | | US 2000-511806 | A3 20000223 |
| | | | US 2001-803516 | A3 20010309 |
| | | | US 2001-999291 | A3 20011115 |
| | | | US 2002-133006 | A3 20020426 |

OTHER SOURCE(S): MARPAT 127:243267

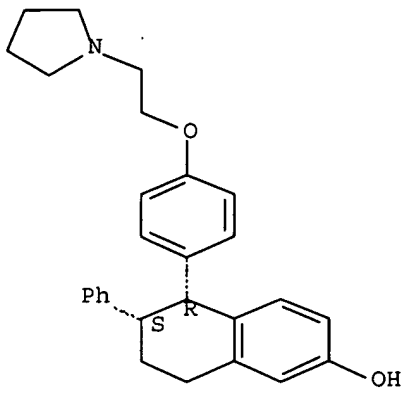
AB Estrogen antagonists or agonists such as cis-6-(4-fluorophenyl)-5-[4-(2-piperidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol are used to treat pathol. conditions such as breast disorder, vaginal atrophy, bladder infection, etc.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen antagonists and estrogen agonists in inhibiting pathol. conditions)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 43 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:600284 HCAPLUS Full-text
DOCUMENT NUMBER: 127:253172
TITLE: Use of 1,1,2-triphenylbut-1-ene derivatives for the manufacture of a medicament for treating Alzheimer's disease
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 792638 | A1 | 19970903 | EP 1997-301146 | 19970221 |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 09315961 | A | 19971209 | JP 1997-40458 | 19970225 |
| CA 2198561 | A1 | 19970828 | CA 1997-2198561 | 19970226 |
| AU 9714965 | A | 19970904 | AU 1997-14965 | 19970227 |
| ZA 9701716 | A | 19980827 | ZA 1997-1716 | 19970227 |
| CN 1165650 | A | 19971126 | CN 1997-103410 | 19970228 |
| PRIORITY APPLN. INFO.: | | | US 1996-25201 P | 19960228 |

OTHER SOURCE(S): MARPAT 127:253172
AB Aminoethoxyphenyl(hydroxyphenyl)phenylbutene derivs. are used in the manufacture of a medicament for the treatment of Alzheimer's Disease. An example compound is droloxifene.

L18 ANSWER 44 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:594636 HCAPLUS Full-text
DOCUMENT NUMBER: 127:257642
TITLE: Combination therapy for osteoporosis with estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists
INVENTOR(S): Ke, Hua Zhu; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9731640 | A1 | 19970904 | WO 1996-IB1462 | 19961223 |
| W: AU, BG, BR, BY, CA, CN, CZ, HU, IL, IS, JP, KR, KZ, LK, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| TW 464496 | B | 20011121 | TW 1996-85115770 | 19961220 |
| CA 2247420 | A1 | 19970904 | CA 1996-2247420 | 19961223 |
| AU 9710398 | A | 19970916 | AU 1997-10398 | 19961223 |
| AU 703285 | B2 | 19990325 | | |
| EP 883404 | A1 | 19981216 | EP 1996-941153 | 19961223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI, RO | | | | |
| CN 1209064 | A | 19990224 | CN 1996-180058 | 19961223 |
| JP 11504352 | T | 19990420 | JP 1997-530738 | 19961223 |
| BR 9612533 | A | 19990720 | BR 1996-12533 | 19961223 |
| HU 9904123 | A2 | 20000528 | HU 1999-4123 | 19961223 |
| NZ 323456 | A | 20010330 | NZ 1996-323456 | 19961223 |
| TR 9801679 | T2 | 20010621 | TR 1998-1679 | 19961223 |
| EP 1236475 | A2 | 20020904 | EP 2002-10920 | 19961223 |
| EP 1236475 | A3 | 20031105 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI, RO | | | | |
| RU 2190395 | C2 | 20021010 | RU 1998-117620 | 19961223 |
| JP 2002308771 | A | 20021023 | JP 2002-54756 | 19961223 |
| PL 187219 | B1 | 20040630 | PL 1996-328831 | 19961223 |
| CN 1515254 | A | 20040728 | CN 2003-10120233 | 19961223 |
| CN 1515316 | A | 20040728 | CN 2003-10120234 | 19961223 |
| CN 1515317 | A | 20040728 | CN 2003-10120235 | 19961223 |
| CN 1515258 | A | 20040728 | CN 2003-10120236 | 19961223 |
| PL 187962 | B1 | 20041130 | PL 1996-359987 | 19961223 |
| CZ 297452 | B6 | 20061213 | CZ 1998-2718 | 19961223 |
| ZA 9701719 | A | 19980827 | ZA 1997-1719 | 19970227 |
| AP 975 | A | 20010612 | AP 2000-1962 | 19970227 |
| W: BW, GM, KE, MW, UG, ZM, ZW | | | | |
| AP 974 | A | 20010612 | AP 1997-934 | 19970227 |
| W: BW, GM, KE, MW, UG, ZM, ZW | | | | |
| US 6323232 | B1 | 20011127 | US 1998-117972 | 19980811 |
| BG 64582 | B1 | 20050831 | BG 1998-102726 | 19980826 |
| NO 9803936 | A | 19980827 | NO 1998-3936 | 19980827 |
| HK 1018210 | A1 | 20060728 | HK 1999-103244 | 19990728 |
| US 2001009920 | A1 | 20010726 | US 2000-736051 | 20001213 |
| AP 1179 | A | 20030630 | AP 2002-2661 | 20021107 |
| W: BW, KE, MW, UG, ZM, ZW | | | | |
| NO 2006003853 | A | 19980827 | NO 2006-3853 | 20060829 |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 1996-12412P | P | 19960228 |
| EP 1996-941153 | A3 | 19961223 |
| JP 1997-530738 | A3 | 19961223 |
| WO 1996-IB1462 | W | 19961223 |
| US 1998-117972 | A3 | 19980811 |

OTHER SOURCE(S): MARPAT 127:257642

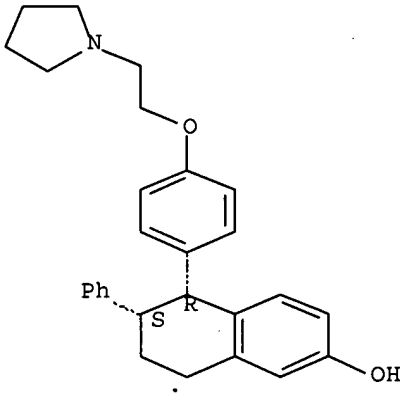
AB Pharmaceutical combination compns. are disclosed which include estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists. The compns. are useful for the treatment of bone disorders including osteoporosis. The effects of PGE2 and droloxifene on bone mineral content and bone mineral d. in ovariectomized rats were determined The data support the strategy of using an anabolic agent to restore bone mass, followed by an anti-resorptive agent to maintain the restored bone mass.

IT 180916-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including osteoporosis)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L18 ANSWER 45 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:589150 HCAPLUS Full-text

DOCUMENT NUMBER: 127:239133

TITLE: Pharmaceutical compositions containing combination of droloxifene and progestins for the treatment of osteoporosis

INVENTOR(S): Maclean, David B.; Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 791356 | A1 | 19970827 | EP 1997-301173 | 19970221 |

R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

| | | | | |
|---|---|---|---|---|
| JP 09315977 | A | 19971209 | JP 1997-39073 | 19970224 |
| CA 2198574 | A1 | 19970828 | CA 1997-2198574 | 19970226 |
| AU 9714967 | A | 19970904 | AU 1997-14967 | 19970227 |
| AU 712656 | B2 | 19991111 | | |
| ZA 9701718 | A | 19980827 | ZA 1997-1718 | 19970227 |
| US 6057309 | A | 20000502 | US 1998-193265 | 19981116 |
| PRIORITY APPLN. INFO.: | | | US 1996-12400P | P 19960228 |
| | | | US 1997-803710 | B1 19970221 |

OTHER SOURCE(S): MARPAT 127:239133

AB Pharmaceutical compns. comprising an effective amount of droloxifene (Markush structure given) or a pharmaceutically acceptable salt thereof together with a progestin are useful for inhibiting bone loss. Tablets containing the above active ingredients 0.25-100, microcryst. cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg each were prepared The efficacy of the combination in treatment of a model of post-menopausal osteoporosis in rats is shown.

L18 ANSWER 46 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:402263 HCAPLUS Full-text

DOCUMENT NUMBER: 111:2263

TITLE: Metabolic activation of eugenol by myeloperoxidase in polymorphonuclear leukocytes

AUTHOR(S): Thompson, David; Constantin-Teodosiu, Despina; Norbeck, Kajsa; Svensson, Bjorn; Moldeus, Peter

CORPORATE SOURCE: Dep. Toxicol., Karolinska Inst., Stockholm, S-104 01, Swed.

SOURCE: Chemical Research in Toxicology (1989), 2(3), 186-92
CODEN: CRTOEC; ISSN: 0893-228X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The metabolism and adverse effects of eugenol (I) in human polymorphonuclear leukocytes (PMN) were studied. Myeloperoxidase, isolated and purified from human PMN, catalyzed the oxidation of I to a reactive intermediate which is likely to be a quinone methide. Eosinophil peroxidase, lactoperoxidase, prostaglandin H synthase, horseradish peroxidase, and rat intestinal peroxidase also supported this H2O2-dependent reaction. GSH inhibited the formation of this metabolite, resulting in the formation of glutathione disulfide and a small amount of I-GSH conjugates. In cellular incubations, phorbol ester stimulated PMN catalyzed the covalent binding of [3H]I to cellular protein, which was partially inhibitable by azide. Intracellular GSH levels decreased by 90% over a period of 30 min in phorbol ester-stimulated PMN exposed to 100 μM I compared with decreases of 30% (phorbol ester alone) or 5% (I alone) in control incubations. In addition, I was more cytotoxic to PMN in the presence of phorbol ester than in its absence, and I inhibited the phorbol ester stimulated oxidative burst in PMN as reflected by a decrease in O consumption, superoxide formation, and H2O2 formation. These results suggest that PMN are capable of activating I to a reactive intermediate and also suggest a mechanism whereby I can potentially interfere with and adversely affect vital PMN functions.

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